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EDITORIAL.

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THE OPEN MEDICAL MIND.

According to our observations and the deeper ones of many acute students, the various minds, which are forces in the thinking world to-day, are striving to break through their narrow bounds, so that a larger view shall be theirs and a keener perception of what is necessary for their continual growth. The medical mind is not in arrear in recognizing what accretions would be of benefit, and yet, though evidences are not wanting to make us hopeful of the future, we must record that of all minds the medical is slower in developing along those lines, which would bring to it the true scientific spirit—the complexion which would have for its greatest virtue the ready understanding of gold and the baser metals, the separating power which can differentiate between grist and chaff. In rebuttal to this statement might be advanced the correct opinion that at no period in the history of medicine have physicians in general taken so active an interest in medico-sociological questions as at present, at no stage in its evolution has a similar willingness been shown to spread a goodly part of the medical feast before the public, so that he who runs may read. But —and here we do not wish to show our disapproval of what has been done, but rather a critical attitude as to the effect of these endeavors on the medical mind—can it be advanced by the unbiased medical looker-on that this confidential front, in regard to the public, has enlarged the medical point of view when brought face to face with discoveries of moment? —medical matters, be it understood, which, were they occurrences in other provinces of thought, would not be long in being accepted at their true valuation. Is it not a fact that our much-vaunted scientific spirit is almost as much warped by our personal feelings to-day as it was in the past,

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and that we still cling to the rather antiquated definition of this same spirit by our almost daily declaration that, for the true essence of medical science to remain the object of our adoration, it must be shielded by the drop-shutters which each and every one of us, who has some knowledge of medicine and a vast amount of experience, has a perfect right to manipulate?

The past year, though no more remarkable in discoveries than many of the preceding years, was illustrative enough of our main point of contention, for though our judgment, if unhampered, would have had sufficient acumen to yield fair play to what had been accomplished in the matter of outstanding achievements, it again gave undeniable evidence of the many incrustations of prejudices and narrownesses, which unfortunately seem never divorced from it. To take but three epochal events,—chemotherapy, the application of radium, and the recognition of psychotherapy,—what have not been the variegated opinions that have been dinned into our ears by those, whose "experience" seemed sufficient justification for the desecration of very good paper by articles that did not stand foursquare but wobbled, since their only support was "an experience" that was pitifully small. But as usual the thinness of the writing was masked sufficiently, for the careless reader, by the fustian thought which always derives such unceasing sustenance from "my cases," "my observations," and especially from "my conclusions."

Of the three subjects, which we have mentioned, none received so shabby a treatment in the American medical press as did that of chemotherapy, as illustrated by Professor Ehrlich's discovery. Directly one or another physician was fortunate enough to receive enough of the preparation to use on a very limited number of cases, his unscientific voice rang through the columns of some journal; and though his knowledge of the technique was declarative of the tyro and his mastery of chemotherapy indicative of the most superficial dabbler, he did not hesitate to visit on the German investigator his failures, though careful all along not to minimize his own share in his successes. Here was an instance of appealing to blind fate for succor in the matter of experimentation, and again compelling the scientific spirit to narrow its field of activity to proportions that could not result in anything else than an inability to judge with percision and accuracy.

When we predicate that the medical mind should be open, we do not advocate its reaching out for every stray bit of flotsam, the outpouring, perhaps, of some misguided and overheated mind that must seek satisfaction in print to assuage its ardor. Such a state of openness would soon be its undoing, for no judgment can be aught but weakened by on-

slaughts, that not only have the grave fault of occurring too often, but are derived with few exceptions from vagarious sources. But what we do mean is a mental condition that bespeaks a receptivity that is tempered by enough critical judgment to make short shrift of the freakish manifestations in medical literature, but is not blind to the worthiness of the things that have the distinctive hall-marks of the out-of-the-ordinary. As the medical mind is constituted to-day it appears to us, in our critical moods, to be a compound of so much that is extraneous and superfluous in the matter of what should be its real make-up, that its acumen is hardly to be depended upon in ferreting out, from the mass of so-called advances, the few wisps which are necessary to the strengthening and broadening of its scientific spirit.

Who has not met with the intellectually small physician, who is so wrapped up in a pet theory of his own that he considers it an attack on his amour-propre to remind him that something outside his sphere is causing a more decided eddying of the waves of thought than his obliquity of vision will admit? This specimen, though barely countenanced by the elect in medical circles, is an entity that must be reckoned with; for though one might at first glance think him an isolated case, and hence not worthy of much thought, a further study will show that he is one of a type that is all too prevalent in our communities. Now it is not that we disapprove of his infatuation of self, or of his resemblance to Dr. Lydgate in "Middlemarch," who was "always making a present of his opinions," for these foibles are shared by quite a number of medical men of decided intellectual force; but what we do deplore is a mental calibre that is just the sort to frown upon all advances in medical science, irrespective of their individual worth. If he could be made "to functionate" within his limitations, the baneful influence which emanates from him might be restricted, but having put a valuation on himself it needs must follow, according to the chronicling of his friends, that he is really a quantity of considerable superiority and that his words should not be scoffed at. The gracious opinions of his friends are just the sort of fuel he needs for his self-concentration, but even though they may have this virtue, is the scientific side of his mind strengthened so that breadth, clarity and sensibility will be its prime qualities? We doubt it.

The matter of the open mind, be it medical or lay, is not a new subject for contemplation or discussion; it has been before us these many years; but not until recently, when the leaven of a mild intellectual socialism was applied to so many accepted matters which our indolence had allowed to lie dormant, did it occur to the few that our mental status was not what it should be. Hence the reformers set to work and the results are not un-

gratifying. But in their enthusiasm to effect the desired changes in the lay mind they took no account of the medical mind or, perhaps, they thought that such reforms, as were desired, should come from within the ranks of medicine. And perhaps they were right in thinking that the medical man, inured as he must be to the shortcomings which should be corrected, would be the keenest critic of the matter, and the most enthusiastic to loosen the medical mind from its moorings and drive it into a clearer atmosphere. But have the printed words of the majority of the articles in our journals, or the spoken words which have fallen on our ears during the past twelvemonth, in connection with the three epochal events mentioned above, betrayed that our medical men have freed themselves entirely from those faults, which were considered undesirable foibles even by our medical forebears?

THE REGULATION OF DIET.

A person in a state of health and ignorance, gets along very well by eating when, what and how much, he chooses. That is to say, with his guardians' and, later, his own, accumulated experience, certain unpleasant experiences teach him a few rough rules as to frequency and amount of food, and the special dangers or inconveniences of certain forms of indulgence. It is true that much of the food that he takes in the belief that it is exceedingly rich in nourishment, such as soups, broths, and the coarse vegetables, is of little value; but the fact that eating is on the whole a pleasant task, there is usually plenty of nourishment from pie, crackers, peanuts, candy, etc.: things which rank very high in food value, but are generally regarded as pleasing to the palate, but more or less harmful.

The average layman, when he acquires a taste of the apple of knowledge, is apt to get very queer notions into his head and, when he attempts to eat by rule, he not only loses much of the reflex digestive stimulation due to appetite, and tends to become neurotic, but is very liable to injure his health directly by following out logical lines of diet unfortunately based on entirely wrong premises. For instance, we have known of a professional glass and metal eater who ate scrambled eggs, alone, to protect the stomach. The orthodox forms of nourishment (?) for convalescents are flavored flour paste, broths and frothy delicacies. Young men frequently overeat, especially of meats and other mainly proteid foods, under the impression that they can thus lay up a stock of energy as one can lay up an excess of money in a bank.

For a person in good general health, it is obviously better to depend on a fairly normal appetite and good luck than on various fallacious beliefs. Undoubtedly, so far as any one nutritive principle is concerned, nourishment by appetite means alternate periods of excess and deficiency, with corresponding loathing of or craving for certain kinds of food. Or, the loathing or craving may be too general to indicate what is required. Hence, probably, arises a large part of the benefit of trips to places where an entirely different dietary, even one apparently injurious, is available.

The state of affairs is very different, however, when we turn out attention from the diet of the hearty, active individual, to the operative case, the fever patient, or the one suffering from some more or less definite metabolic disease. Not to mention physiological and professional considerations, a regard for common honesty ought to condemn the physician who says, off-hand, to a hard-working, nervously-exhausted man, in winter: "Take nothing but milk, for a month;" or the one who considers it is worth two dollars to tell a man not to eat pie; or the one who, after doing a gastrostomy or enterostomy to prevent a patient from starving, prescribes a few cubic centimeters of a 5 per cent. solution of albumin three times a day; or the one who, having no idea of heat units, measures of weight or volume, is ignorant as to how much is required to prevent starvation in a typhoid patient.

Few physicians realize how important a branch of therapeutics, dietetics is, nor how far the armamentarium of the grocery and butcher shop may replace that of the drug store. Starting with baking powder and ending with cranberries and other vegetable products rich in benzoic acid, one could even treat gonorrhea dietetically, rather slowly and with a large percentage of failures, but still a good deal better than it has been treated by many a drug-user, up to the last few years. Animal extracts all properly come within the field of dietetics. We may state a personal practice for what it is worth: for years, the writer has practically never given cod liver oil but an abundance—though not an excess—of the ordinary, more delicate fatty and oily foods; also, that in the treatment of anemias, he has prescribed iron at the butcher's in nearly every case. Tea, coffee, chocolate, tobacco, spices and the saline and acid substances used in cooking or accidentally present in food stuffs, make up quite an extensive armamentarium.

Still, such phases of dietetics are of greater interest for speculation than matters of practical importance. The gist of dietetics, as regards the three classes of organic nutrients: proteid, carbohydrate and fat, is the furnishing of energy and reparative material to the body.

There is no royal road to dietetic skill. One must know how foods are

used in the body, how much is needed, and how much of each nutrient is contained in each food stuff. As in the case of medicinal therapeutics, one must study physiology, memorize doses, and, since for reasons not fully understood and requiring lengthy discussion, nutrition cannot be satisfactorily carried on by isolated, proximate principles, one must memorize the proportionate amounts of such principles in the individual food stuff, just as one must know the percentage of an active principle in a crude drug.

This means hard work, but by no means so hard as in the case of medicinal therapeutics; for the number of active ingredients are relatively few in dietetics and the raw food stuffs are much more amenable to classification.

OPINION AND CRITICISM.

A MODERN INTERPRETATION OF PLAY.

The tendency of a number of modern writers, when they wish to call particular attention to their subject-matter, or rather when they wish to explain the psychology of an act or a people, is not to follow in the beaten paths as regards titles, and carelessly name a book or article without special reference to the manner of the context, but to make the top-line illuminative of what is to follow. Thus, quite recently, we have read Havelock Ellis's "The Soul of Spain," Washburn's "Pages from the Book of Paris," which has been advertised as "The Soul of Paris in Word and Picture," and Dr. Richard C. Cabot's "The Soul of Play" in the *Atlantic Monthly* for November. Hence we see that the understanding of any subject is really very superficial until we get at its soul, and that this is not matter for derision is well shown in the Ellis book and, especially, in Dr. Cabot's penetrating study of play.

According to Dr. Cabot, we Americans know but little of the true definition of life as it should be, for in our hurry to acquire money we have concentrated all our forces on work, and have relegated to a deplorably insignificant position both recreation and affection. This thought will come as news to all those Americans, who have imagined themselves for years the greatest people on earth, not only on account of their prosperity, but because a special providence of their own ordering was supposed by them to have granted them all the benefits which could possibly fall to mankind. That they have been living in a delusive state, in regard to what should constitute happiness, is now made clear to us by Dr. Cabot in language that is restrained, yet at the same time forceful; and when the presentation of a subject is done so effectively and so impartially should we not at once admit that here is no over-statement of facts?

The topic which engages Dr. Cabot's attention is the matter of recreation, and not affection, for as he pertinently says, "some day perhaps a conference will be called to study, to nourish, and to conserve the other great life-force,—to the end that we may be less 'stupid in the affections.'" And with this dismissal of affection he plunges into the subject of recreation, and shows us in a short space of time that play need not necessarily be a waste of time, but the means by which we re-create our beings from depression into a more healthful state. For if relaxation can re-create—and who can doubt this even though the experience has been limited—a goal is attained that makes us saner beings, and deprives us of all those

crotchets with which work undiverted with play cobwebs our overtaxed brains.

As we understand Dr. Cabot's words, the soul of play is recreation, and this force is achieved not by athleticism, or the indulgence in a sport that must entail physical and mental depression, but by imbibing without effort the pleasant things around us; in fact, making of this effortless period in our stressful existence a cult of the most agreeable sensations: grace that pleases the eye and sounds that soothe, through the sense of hearing, the distraction wrought by the preceding hours.

Despite our belief in the truths of Dr. Cabot's paper, we feel that what he says will fall on indifferent ears, for the typical American will be loath to submit to this inactivity, though the results may be soothing enough. As we know him—and our knowledge is not restricted—quiescence is about the most difficult state for him to tolerate. Perhaps his ambition to be doing something, even when there is nothing to do, may be responsible for his dislike of quietude at any time, but what is really at the root of his restlessness is the unquenchable desire not to be second in any race, though the competition may, as in this instance, bring but few guerdons wherewith to garnish his reputation. He has evidenced this attitude in business, in sport and in athletics; so why should he be different when he engages in the new "sport" advocated by Dr. Cabot—relaxation and re-creation?

SCIENCE VS. ROMANCE.

A merely superficial estimate of the literary (?) output, during the past year, on the alluring subject of how to prevent sexual diseases, convinces us that many minds are working on the same subject, though unfortunately in so many directions that bewilderment is the result in many readers' minds. If there is any human brain large enough to hold all the theories and advice which have been gratuitously flung at us by all those who would think it a fatal mistake to allow the ink on their pens to dry, even for a moment, we have never come across it in our peregrinations; but then we may not have been looking for it; in fact, may have been so frivolous, even when science enthralled us, that its escape from our attention was predetermined. The young man of to-day, according to these medical philosophers, must arrive at a higher standard of morality or immorality,—it is not clear whether sexual intercourse without benefit of clergy must stop altogether or whether preventive measures, that will make this sort of sexuality less disturbing some weeks after, is the thing advocated,—and to reach these empyrean heights all that is necessary is for him to acquire the simplistic rules laid down by

one or another author or—and here our brain of limited capacity stands aghast—digest all the regulations which have appeared up to date.

Simplicity in the presentation of medical subjects has never been their strongest asset; but what directness, what clarity is in the purely medical article by comparison with the manner of the medico-sociological writers on sexual matters when divulging their many involved ideas as to what must be done by the aforesaid young man if the world is to be regenerated! Yes, undoubtedly, it is the young man upon whom all responsibility rests as regards the abolition of sexual diseases; and if he would listen to the preachments of the authors, if he would but remember why prostitution exists, why it is wrong for him to desire illicit intercourse, why he should divert his thought to other and healthier things, what preventive measures he should use should the overpowering desire seize him despite his high resolves, what the priceless value of judgment is in the matter of knowing when to refrain, and a few hundred other confidential "I told you so's," great will be his gain; but no greater than the world's, for out of the purity of his life will come so delightful a period of peace and content for all beings here on earth that the fervent will no longer desire the millennium.

To effect this complete palingenesis of the young man has been the dominant note in quite a number of articles and books, and though we are sceptical as to its fulfillment, there is even with us the wish that it might be so. But it is an altogether different matter when advice is given as to how to prevent sexual diseases, especially when the advice is such that to follow it out to the letter would entail many minutes of uninterrupted labor. Here our scepticism would be rampant, for if fulfillment of the task were ever accomplished, it would be at the cost of all thought of prospective intercourse. Listen to the wise words of Dr. Victor C. Vecki ("The Prevention of Sexual Diseases"), who appears to be a modern Pepys of the alcove: "Before the act the sexual parts must first be washed thoroughly with hot water and soap, cold water to be used in preference to none; then the parts and surroundings, including the whole scrotum, liberally anointed with the calomel salve. After the act it is necessary to urinate, then another thorough washing and a careful rubbing in of the same salve. The washing and lubricating must comprise every fold and recess, not to forget the space below the frenulum. After the washing and rubbing in of the calomel salve, a few drops of the nitrate of silver solution are deposited in the meatus, which is for this purpose caused to gape as far as possible."

Since there is no exact time mentioned when the washing and rubbing in of the calomel salve should take place—the author vaguely states "before the act"—we take it that to be most effective it should be done in the inamorata's house or room. Of course, this interpretation on our part is taking great liberties with the author's text,—we certainly must be wrong, since so well read a man as Dr. Vecki cannot possibly be un-

acquainted with Havelock Ellis's chapters on "The Evolution of Modesty," "Analysis of the Sexual Impulse," and "The Sexual Impulse in Women,"—for he may mean that the young man should make all preparations in his own home and sally forth for his quarry only after being thoroughly cleansed and salved. The spectacle of a number of young men thus "made up," undergoing all the mental tortures of an ataxic walk to prevent the ointment from becoming dislodged, would surely add to the gaiety of our otherwise humdrum streets.

LITERARY NOTE.

In Jane Addams' most recent publication, "Twenty Years at Hull-House," the reader will find enough to interest him, in case his predilections run in the ever-widening groove of settlement work. For here are told, not only the early and rather discouraging experiences of a worker whose persistency and single-heartedness are not her least qualities, but also the later experiences which were less discouraging, for then appreciation and encouragement were meted out in no stinted manner. Hull-House embodies in all its details the individuality of its progenitress; and it is well that this should be, for the history of most charities is only too often a sorry affair, since disorder and collapse are their most grievous chapter, on account of the wrangling which ensues from the absence of a master-mind. No such charge can be brought against Hull-House, for, during its uninterrupted career of twenty years, the guiding hand has not only been the same, but it has never wavered in directing the onward march of this institution to its present almost perfect goal. Hence the great lesson to be learned from the career of this woman, by all medical readers, is that only when an individual at the head of a charity has the ability to exercise perfect mastery is success assured; a fact, which has never been brought home to all medical thinkers in a more lucid manner than in Dr. Lauriston E. Shaw's Address on The Disorder of Medical Charity, delivered before the Stratford Division of the British Medical Association on November 3rd, 1910. Aside from what the book tells us of the uplift which has been diffused, from this centre of concentrated thought, throughout the many foreign neighborhoods which surround it, it has the right sort of literary grace, since here is illustrated Buffon's apothegm—namely, "The style is the man" or the woman, as it would be in this case.

ORIGINAL ARTICLES.

THE PRESENT STATUS OF THE NOGUCHI SYSTEM OF SERODIAGNOSIS OF SYPHILIS.

By Hideyo Noguchi, M. D., of the Rockefeller Institute for Medical Research, New York.

In 1909 I introduced a method of complement fixation-test for syphilis along the same line upon which the Wassermann test is founded. The construction of my method deviates, however, from the original in that there is in my method but little of what was originally incorporated by Wassermann. The reaction is the same by both methods, but the reagents employed in the two are quite different, and the theoretical and practical consequences arising from the differences in the reagents are matters which are of considerable importance.

When the Wassermann reaction was discovered and found to be of great aid in the diagnosis of syphilis, the medical profession was anxious to derive as much benefit from it as possible; but the difficulties associated with the preparation and the execution of the original method were too great for the test to be used beyond a narrow circle of investigators.

In order to render the test less cumbersome, attempts were made by different investigators to modify the technique so that a greater degree of simplicity might be attained. Thus one modification after another was proposed and tried from time to time, yet, unfortunately, they all failed because they were mostly the result of hasty performance and lacked proper scientific foundation. The chief cause of failure, on the part of the investigators, was that they concentrated their thought on simplification and regarded the question of accuracy as a matter of secondary importance. In my opinion, these modifications were not successful even as regards simplification, since the reagents employed were just as unreliable as in the Wassermann method, and the carrying-out of the test required the same knowledge of serology, which was the important point in the original method. The disappointment which prevailed in medical circles after these modifications were found to be failures was a severe blow to progress in the matter of simplifying the Wassermann method; and, even to-day, any modification, no matter how carefully constructed, arouses a degree of scepticism, on account of the

fixed idea in the medical mind that no improvement on the Wassermann method is possible, since all previous attempts were failures.

Despite these setbacks the science of serology is now making a steady advance. And this advance is only possible if the serologists apply themselves, in the best scientific manner, to the construction of methods which are theoretically more accurate, practically more delicate, and technically simpler than the complicated methods, which, by reason of their lack of simplicity, cannot be generally adopted.

The method which I introduced met at first with some adverse criticism and the result of this was that its general usage was limited, but all obstacles were removed one by one when its practical points were fully established. To-day I am justified in stating that the reliability of my method has been confirmed by all those who have adopted it.

In order to enable the reader to understand the differences between the original Wassermann reaction and my method, a brief comparison of the two is given below.

A. Reagents for the Test.

WASSERMANN'S METHOD.	NOGUCHI'S METHOD.
Serum of Patient— Must be heated to 56°C. for 30 minutes before being used for the test. Requires ten times more serum than in the Noguchi method. Procured usually from a vein.	Heating at 56°C. not necessary, although an inactivated specimen can also be used. One-tenth of the amount that is required in the original is sufficient. Procured usually from a finger or ear lobe.
Antigen— Must be prepared from the liver of a congenital fetus, which is not always suitable for use. Selection of suitable preparations is essential. The mode of standardization is based upon an empirical basis.	Can be prepared from the liver, heart or kidney of man, beef, sheep, rabbit, etc. Selection of suitable preparations is essential by a special standardization formulated by me. It is, however, comparatively simple and has a biochemical basis.
Deteriorates rapidly and often suddenly. The titration of the antigen every time before making the test is empirical. It is seldom that it remains unaltered longer than a few weeks. Recently certain workers employ an alcoholic extract instead of an aqueous extract, but Wassermann still opposes this modification.	Deteriorates very slowly and never in a sudden manner. In an alcoholic stock solution it remains unaltered for at least one year. From this stock solution any quantity of emulsion can be prepared at the time of use.
Complement— Guinea-pig's fresh blood-serum.	Same as the original, only used in 2½ times less quantity.
Blood-Corpuscles— Washed corpuscles of *sheep* blood, 1 c.c. of 5 per cent. suspension.	Washed *human* corpuscles, either 0.1 c.c. of 10 per cent. suspension or 1 c.c. of 1 per cent. suspension. Patient's corpuscles can be used for this purpose, thus one patient can supply enough suspension of corpuscles for the others as well. There is no necessity of obtaining blood corpuscles from a normal individual.

Amboceptor—

Immune serum of rabbit repeatedly injected with washed *sheep* corpuscles. It is essential to keep the serum on ice. Aseptic precaution is strictly necessary. A frequent titration is absolutely essential.

Immune serum of rabbit repeatedly injected with washed *human* corpuscles. When dried on paper it remains active for at least one year, and it seldom deteriorates in this form even when kept at room temperature. No asepsis is necessary. A frequent titration is not necessary.

B. Time Required for Carrying Out the Test.

WASSERMANN'S METHOD.	NOGUCHI'S METHOD.
Preliminary Tests— The antigen, complement, and the amboceptor must be titrated just before making the main test. This requires, at least, two hours in the hands of an expert.	The preliminary tests are not necessary for the reason that the most changeable reagents such as antigen and amboceptor are in a stable form in this method. It is of course understood that once or twice in one month they should be titrated so as to ascertain their activity.
Main Test— The test for the diagnosis is to be commenced after the preliminary tests. The main test requires about *twenty-four hours before the results can be recorded.* The actual time spent for manipulation and watching is about three hours.	The main test is directly commenced. When a water thermostat is used the final outcome of the test can be recorded within *two hours.*

C. Qualification for Preparing the Reagents and Performing the Test.

In the original Wassermann method the reagents necessary for making the test must be prepared by those who are going to use them. The difficulties in handling these most changeable reagents demand a man of great ability and wide experience in this special field of work. He must also be an expert serologist; not one who occasionally does a Wassermann reaction, but one who devotes himself constantly to this line of work. No man should attempt to make a responsible test unless he is capable of preparing these reagents. In this method the preparation and performance of the test are *inseparable.*

In the Noguchi method the preparation of the reagents and the performance of the test can be *separated.* While the preparation of the reagents is to be entrusted to a skilled serologist, the performance of the test may be made by a physician who has had a certain amount of laboratory training and has gained enough experience in the actual technique for doing the reaction. The performer must, of course, understand thoroughly the properties of each reagent in use, and be familiar with various irregularities which may arise during the performance of the test, but all these requirements can be fulfilled by a beginner after he has done a few hundreds of tests. He is urgently warned against considering himself competent before a few months' training with the technique. This warning applies equally to regular laboratory workers.

D. Certain Important Serological Considerations Affecting the Result.

Where Lies the Cause for a Negative Wassermann with a Positive Noguchi?—This phenomenon seldom occurs. It occurs with a specimen

of serum in which an enormous amount of the natural hemolytic amboceptor for the sheep corpuscles is present. One must not forget that a positive reaction can be easily made negative by adding more amboceptor to the test-tube. This is produced through the augmenting effect of the amboceptor in excess upon the activity of the complement. The same amount of complement can produce two entirely different amounts of hemolysis, when mixed with a smaller or larger amount of the amboceptor. Thus, an excess of amboceptor can convert a positive reaction into a negative or, at least, into a weaker. In human sera there exist variable quantities of natural amboceptor for the sheep corpuscles, but not for human corpuscles. Since the Wassermann method uses the sheep cells and the Noguchi the human cells, it sometimes happens that the reaction is negative with the Wassermann and positive with the Noguchi.

As the amount of the amboceptor in the Wassermann method becomes unknown through the presence of the natural anti-sheep amboceptor in the serum to be tested, it is quite irrational to titrate the complement, the activity of which becomes so different according to the amount of the amboceptor. This throws the quantitative meaning out of the Wassermann method. With the Noguchi method no such disturbance can result.

In building up the complement fixation-test on a quantitative foundation the Wassermann method has a very serious obstacle, because the amount of the amboceptor in that method is unknown, and, if it be determined by a special experiment, it cannot be removed from such a serum.

How to Avoid a Non-specific Positive Reaction with Unheated Human Sera.—It is most important to know that, when used in active states, certain specimens of human sera give a positive reaction with the antigens containing proteins. Thus, the antigens prepared by the method of Wassermann, or by extracting the tissues with alcohol, are unsuitable for use with the unheated human sera. In order to avoid this non-specific positive reaction I have recommended the use of pure lipoids consisting of phosphatids prepared by my method. In this form the antigen never gives the non-specific fixation with active human sera, yet the reaction with syphilitic sera is extremely sensitive. A few early workers, all without sufficient experience with my method, obtained a non-specific fixation with some active human sera, but they invariably neglected this vital precaution. There is no man now who obtains such a disastrous result and then rushes into print.

Some might ask why I do not take the native human complement (which is present in an unheated fresh specimen) into consideration. In answer to this question I must inform the inquirer that the human complement contained in the amount of serum I recommend in my method, is so weak that even *ten times* more of it cannot act upon the human corpuscles in the presence of the amboceptor therein employed. This does not apply to any other heterohemolytic system in which alien corpuscles

(such as those of the sheep) are employed. In *that* instance human complement is highly active.

Certain modifications (Hecht, Stern, Tschernogubow) of the Wassermann method use the complement of the patient, and hence the serum in active state. But, owing to the lack of knowledge in regard to the non-specific fixation, these authors employed the crude alcoholic extract as antigen. This resulted in obtaining occasional positive reactions with non-specific cases. I know that they could have avoided this difficulty by adopting my way of preparing the antigen. Criticism arose from various places against the use of an active serum for the test and this is fully justified. But, when one tries to criticize my method because of the use of active serum one errs, since I have long avoided this source of error by eliminating the proteins from the antigen.

Standardization of the Antigen.—In the Wassermann method as well as in almost all the other modifications (those which follow the original without any further investigation), the amount of the antigen-extract for the test is so regulated that the half of the quantity, which causes self-inhibition of hemolysis, is taken and tested with a large number of non-syphilitic and syphilitic sera, to see whether or not it gives a positive reaction with syphilis and a negative reaction with non-syphilitic sera. If it gives a positive reaction for syphilitic sera only in this quantity, the extract is declared suitable as antigen. Thus, to establish whether a given extract is suitable or not it takes a considerable length of time and a large number of specimens. This is based purely upon empiricism.

Let us now consider how difficult it is for average workers to select a suitable antigen in this way. It should be remembered that a positive reaction may be obtained with only *one unit of antigenic activity* or with *several*. With a strong serum, containing a large amount of the so-called syphilitic antibody, the reaction is the same, whether one or several antigenic units are employed. On the other hand, a weaker positive serum will give a complete positive reaction with *several* antigenic units, but only a slightly positive or even a negative reaction with *one* antigenic unit (as determined with a strong serum). From this one can easily see that different investigators are liable to employ various numbers of antigenic units. Under such conditions it is no wonder that the results often vary according to different workers. It really calls for the establishment of a more definite standard for the antigen.

In my method I have recently set forth a definite standard of antigen, and it requires only a comparatively short time to decide whether a given preparation is suitable or not. Briefly stated it is as follows: Take 1 part of a 3 per cent. solution of the aceton-insoluble tissue lipoid in methyl alcohol (stock solution) and mix with 9 parts of physiological salt solution. This will become an opalescent emulsion ready for determination. 1. Determine if the emulsion exerts any hemolytic action upon human corpuscles by using 0.4 c.c. of the emulsion upon the regular amount

of corpuscles for my method. If it is hemolytic the emulsion is to be discarded as unsuitable. 2. Determine if the emulsion in 0.4 c.c. is anticomplementary or not. If it is anticomplementary the emulsion is not suitable. When the emulsion is neither hemolytic nor anticomplementary we finally determine it for (3) the antigenic strength. In this determination the amount of the syphilitic serum should be that which gives complete fixation with a standard antigen (already in hand). Now take 0.02 c.c. of the emulsion just mentioned and make the regular fixation experiment with that syphilitic serum. If the hemolysis is completely stopped (positive reaction) with this quantity, the emulsion is suitable and should be used in 0.1 c.c. for the real test for diagnosis. The reason why I employ 0.1 c.c. of the emulsion in the test is to have at least 5 antigenic units $\left(\frac{0.1}{0.02}=5 \text{ units}\right)$, so that even the weakest reaction cannot escape the detection. At the same time it is guarded from the hypersensitiveness of the reaction, because I have found, as experimental bases, that nonsyphilitic sera do not give a positive reaction even with 0.4 c.c. of such an emulsion. The reason why I do not recommend more than 0.1 c.c. for one test is that no matter how many more antigenic units above a certain number (3 to 4 antigenic units) are employed, the reactions of varying degrees remain unaffected. We are, therefore, employing the maximum of the antigenic emulsion and the results are revealed to the utmost.

It does not matter whether the lipoids are obtained from man, animal or whatsoever tissue, so long as the three important properties (hemolytic, anticomplementary and antigenic) are determined according to the standard above given. The procedures for these determinations are certainly quite simple, yet they are based upon a definite biochemical foundation.

It may not be superfluous at this place to point out still other reasons why I came to employ the aceton-insoluble lipoids. In aqueous as well as in alcoholic extracts of tissues (especially autolysed organs, such as macerated fetal liver), there exists a large number of hemolytic and anticomplementary substances. With an aqueous extract it is easy to understand why the complement is completely fixed when the quantity of the extract exceeds a certain limit. The various proteins in colloidal state absorb the complement (so-called absorption phenomenon), a well-known fact since the time of Wild. For this reason an aqueous extract cannot be used beyond certain quantities. It often contains hemolytic substances, and cannot be used for this undesirable auxilliary action. With the crude alcoholic extract the amount of proteins is not so great as in the aqueous, but it contains certain other substances which remain inert in the aqueous but reveal their actions after being taken up by alcohol. These substances are soaps (highly hemolytic), neutral fat, various

fatty acids (the latter highly hemolytic and anticomplementary), cholesterin, etc. Owing to their presence the alcoholic extract cannot be used in a large quantity. It is not infrequent that a crude alcoholic extract is so hemolytic that it cannot be tested for the antigenic strength.

Contrasted with the aqueous and alcoholic (unfractionated) extracts the aceton-insoluble lipoids are usually non-hemolytic and only slightly anticomplementary, if at all. The antigenic property is strikingly strong with the majority of the preparations of these lipoids. As there are certain specimens which are exceptional to this, it becomes necessary to make selection of a suitable one by the method already outlined. For the technical details the reader is referred to my work which has just appeared.

In concluding this topic, I may mention the fact that, in the standard of suitable antigen for the Wassermann, the difference between the anticomplementary and antigenic doses of the extract is 211 or more (undetermined), while in my method the difference between the two is, at least, $20:1\ \left(\frac{0.4}{0.02}=20\right)$.

Concerning the Estimation of the Strength of Reaction.—When the complement is completely fixed by the syphilitic serum and antigen, it is said to be positive or, according to certain investigators, strongly positive. But, who knows whether the same is caused by just that quantity of syphilitic antibody sufficient to fix that amount of complement or by a considerable excess of the antibody, unless a further analysis is made.

In the Wassermann method Citron introduced a method by which he aimed to estimate the strength of the reaction. His idea is to combine two different quantities (0.2 c.c. and 0.1 c.c.) of the patient's serum with two different quantities (0.2 c.c. and 0.1 c.c.) of antigen extract. When complete inhibition occurs with the smallest amount of patient's serum and that of the antigen, it is recorded + + + +, etc., until an imperfect inhibition with the largest quantity of both is designated as ±, or doubtful reaction. He divides the intensity into + + + +, + + +, + +, +, ±. It will be seen from the above that my method approaches the ideal of a quantitative method.

I have examined a large number (over 100) of sera from cases of syphilis treated with Ehrlich-Hata's "606," by this quantitative method. In certain instances we could detect the relapse, though clinical symptoms were no longer in evidence at the time.

The quantity of the serum required for a complete quantitative analysis by this method is only 0.1 c.c. On the other hand, the methods of Citron and Zeissler demand, at least, several cubic centimeters.

Where Other Modifications Stand in Serology.—In this connection I may also review, from the quantitative standpoint, one or two other modifications now in use in certain parts of Europe. The modifications

of Hecht, Stern, Tschernogubow, Foix, etc., utilize the complement of the serum of the patient under investigation. In these modifications the human complement contained in the specimen of serum takes the place of the guinea-pig's complement used in the original, as well as in my method. When the specimen gets old the native complement gradually deteriorates and no examination can be made with such a serum. It is absolutely necessary to examine the serum, while it is perfectly fresh, as the complement is a very unreliable substance. In the fresh state the amount of human complement in different specimens varies more or less, often considerably. Hence these investigators are working with an undetermined amount of complement. Besides, human serum contains various quantities of natural amboceptors against the alien corpuscles employed by them (sheep—Stern, Hecht; guinea-pig—Tschernogubow; rabbit—Foix), and the experimenters are in the dark as to the exact amount of the amboceptors they are utilizing.

The uncertainty of the quantities of complement and amboceptor is sufficient to show that these modifications are not suitable for any accurate quantitative work. Yet another thought, in regard to the impossibility of making any attempt to estimate the strength of the reaction, may be of some benefit for those who are in habit of considering every modification as *about* the same. With these modifications it is absolutely impossible to estimate the strength of reaction by using a smaller quantity of the patient's serum, because on dilution the serum loses rapidly and progressively the strength of complement and amboceptor so that hemolysis can no longer be produced,—and without a hemolytic system there is no fixation-test. Is it still fair for a critic to classify my method with these unserological methods, simply because it is called a modification like the others? In truth, my method is very little of a modification; and having been constructed chiefly upon an entirely new series of experimental investigations and observations, it is quite inadequate in revealing a still stronger reaction. I have met with such specimens of sera which gave still complete fixation in quantities as small as 0.0006, 0.001, 0.005, etc. The smallest quantity used in Citron's estimation is 0.1 c.c. Another point of uncertainty in this scheme is that the number of the antigenic *units* in a given *volume* of the extract can vary so greatly that a uniform result comparable with one another is scarcely to be hoped for. Again, with regard to estimating a weaker reaction, it is not to be overlooked that the variations in the amounts of the amboceptor in each specimen alone can bring about any degree of reaction, without any relation to the actual amount of the so-called syphilitic antibody contained in the serum. In other words, the same amount of the antibody may give + + + +, + + +, + +, +, ±, or—, depending upon the amount of the natural antisheep amboceptor.

Zeissler's plan runs in the same direction as that proposed by Citron, and cannot be considered quantitatively correct. The complement fixa-

tion-test carried out by my method permits, however, a fairly accurate estimation of the strength of the reaction. In this method we have a definite quantity, under perfect control, of four out of the five factors concerned in the reaction. It is not difficult to derive the value of one unknown factor when the other four factors are quantitatively known. Thus, we know the exact amounts of antigen, complement, amboceptor and corpuscles, and can easily determine the amount of the antibody contained in a given specimen of syphilitic serum. I prepare a series of test-tubes, and measure gradually decreasing quantities of the patient's serum into them. With these varying quantities of the serum I make the fixation-test in the usual way. By this means we are bound to find out the smallest amount of the serum which still produces complete fixation of the complement. This quantity of the serum contains *one* unit of the syphilitic antibody. Thus, by dividing the quantity of the serum recommended for routine work, that is, 0.02 c.c. of active serum, with the *titer* of a given specimen, one derives the number of the syphilitic antibodies examined in that serum. For example, a syphilitic serum which gives a positive reaction in quantity of 0.002 c.c. contains 10 antibody units $\left(\frac{0.02}{0.002}=10\right)$. A specimen with the titer of 0.006 c.c. contains 3.3 units $\left(\frac{0.02}{0.006}=3.3\right)$, and so forth. There is not a single factor in my method which is in common with that found in the Wassermann method. In fact, it is a complete reconstruction of the entire process of the complement fixation-test for syphilis. To reconstruct a method after the manner of the newer investigations, which do not lack in strength, and thereby remove certain defects of the original is not the same thing as to omit one factor or combine more than two factors in one single medium, as is commonly done in these modifications, so as to reduce the technical labor necessary for the original method at the expense of the accuracy of the test. It reminds me of an invalid who, although most useful, is too heavy to be carried around and has one or two limbs amputated to lessen the burden. The invalid still works, but with a reduced efficiency. Notwithstanding the omission of one factor or combination of more than two factors in one medium, the labor and time consumed for carrying out these modifications are not at all economized. The preparation of the reagents and the performance of the test demand a man capable of doing both. Thus the aim of these investigators is not attained.

E. What has the Noguchi Method Accomplished?

It is this phase of the subject which would interest the majority of the readers of this journal most. The most important practical question of the test is not whether it is easy to carry out, but whether it

TABLE I.

The results obtained with the Noguchi method in Syphilis.

		Primary Syphilis			Secondary Syphilis			Tertiary Syphilis			Latent Syphilis			Congenital Syphilis			Cerebrospinal Syphilis			
		No. of Cases.	W. %	N. %	No. of Cases.	W. %	N. %	No. of Cases.	W. %	N. %	No. of Cases.	W. %	N. %	No. of Cases.	W. %	N. %	No. of Cases.	W. %	N. %	Total.
Comparison with the Wassermann method.	Noguchi	23	73.9	86.9	79	83.7	96.2	65	80.0	87.6	59	61.0	75.5	4	100.0	100.0	5	....	80.0	235
	Fox	7	100.0	100.0	37	97.0	100.0	32	71.0	84.0	54	46.0	62.0	1	100.0	100.0	..	....	....	131
	Kaplan	138	90.0	97.0	281	86.0	98.0	191	73.0	81.0	79	51.0	75.0	20	90.0	90.0	..	....	....	709
	Swift	16	81.0	81.0	76	92.0	97.0	45	80.0	88.0	85	55.0	62.0	4	100.0	100.0	..	....	....	226
	Corson-White	14	86.0	100.0	146	98.0	99.0	47	80.0	80.0	28	60.0	64.0	39	100.0	100.0	35	80.0	80.0	309
	Kaliski	10	100.0	100.0	50‡	94.0	100.0	75§	60.0	80.0	..	....	....	11	100.0	100.0	15	66.0	80.0	161
	Total	208	88.0	94.0	669	92.0	98.0	455	74.0	83.0	305	54.0	68.0	79	98.0	98.0	55	73.0	80.0	1771
Without comparison	Noguchi	70	....	92.8	197	....	96.0	177	....	88.9	270	....	74.4	17	....	100.0	5	....	100.0	736
	Craig	90	....	72.0*	163	....	88.0	74	....	82.0	55	....	72.0	9	....	88.8	..	....	.....	491
	Orleman-Robinson	29	....	86.0	48	....	93.0	60	....	80.0	33	....	69.6	10	....	100.0	..	....	.....	180
	Potter (Alf.)	7	....	86.0	71	....	98.6	46	....	78.0	58	....	66.0	..	....	.....	..	....	.....	182
	Groat	12	....	100.0	76	....	94.7	36	....	70.0	51	....	40.0†	10	....	100.0	1	....	100.0	186
	Berghausen	..	....	.....	15	....	93.0	9	....	88.0	6	....	66.0	4	....	75.0	..	....	.....	34
	Total	208	....	87.5	570	....	94.7	402	....	82.8	474	....	64.6	50	....	93.0	6	....	100.0	1809
	Grand total	416	88.0	90.0	1239	92.0	96.0	857	74.0	83.0	779	54.0	66.3	129	98.0	96.0	61	73.0	90.0	3580

*Includes very early cases. †Majority under treatment. ‡Untreated. §Includes latent cases. W.-Wassermann method. N.-Noguchi method.

gives a reliable result as a diagnostic means. My system has been put to practical trial for nearly two years and applied to at least 10,000 cases of syphilis, parasyphilis, and various other non-syphilitic diseases. The same method has been adopted at different medical schools and hospitals, and is being introduced gradually into numerous clinical laboratories, where the original Wassermann method is not thought of being done. The Army and Navy Medical Schools of the United States have been using the test for some time. The Pasteur Institute of Paris has also adopted my method to the exclusion of all others. All the State Hospitals of New York, as well as a number of State Hospitals in other States, are employing it. So far as I am aware these investigators are not having any difficulty in obtaining uniform and reliable results.

TABLE II.

		General Paralysis					
		Blood serum			Cerebrospinal fluid		
		No. of Cases.	W. %	N. %	No. of Cases.	W. %	N. %
Compared with the Wassermann method.	Corson-White	11	80	80	5	100	100
	Kaplan	61	65	72	..	...	...
	Kaliski	3	66	66	..	...	...
	Total	75	70	73	5	100	100
Without comparison	Rosanoff and Wiseman	56	..	80	44	...	86
	Noguchi	25	..	86	..	...	...
	Schradieck	4	..	100	..	...	...
	Groat	2	..	100	..	...	...
	Total	87	..	91	44	...	86
	Grand Total	162	70	73.4	49	100	93

		Tabes		
		Blood serum		
		No. of Cases	W. %	N. %
Compared with the Wassermann method.	Noguchi	8	44	72
	Kaplan	205	60	65
	Corson-White	49	70	75
	Kaliski	10	40	60
	Berghausen	6	...	66
	Fox	3	100	100
Without comparison	Noguchi	125	...	68
	Waugh	13	...	56
	Total	419	62.8	72

Syphilis and Parasyphilis.—In Tables I. and II. one sees that the percentages of positive reactions in syphilitic and parasyphilitic conditions are somewhat higher with my method, as compared with the results obtained with the Wassermann method in the same cases, when simultaneously examined by both.

The reason why my method is sometimes positive when Wassermann's may be negative has been fully explained in the theoretical considerations of this article, but the following results obtained by Kaliski may be interesting for the reader, as examples:—

TABLE III.

NOGUCHI METHOD POSITIVE, WASSERMANN NEGATIVE.

	N.	W.	
Congenital syphilis	+	—	Under Hg treatment till recently.
Secondary syphilis	×	—	Under Hg treatment till 3 months ago.
Secondary syphilis	+	×	Under Hg treatment.
Latent syphilis	×	—	Chancre many years ago.
Tertiary syphilis	×	—	
Tertiary syphilis	+	×	Excess natural antisheep amboceptor.
Tertiary syphilis	+	—	Gumma pyloric end stomach.
Tertiary syphilis	×	—	Under Hg treatment.
Latent syphilis	×	—	Chronic intermittent treatment 7 years.
Cerebrospinal syphilis	+	—	
Cerebrospinal syphilis	+	=	Wassermann almost negative.
Cerebrospinal syphilis	+	=	Wassermann only suspicious.
Aphasia	+	—	
Tabes	+	—	Great excess antisheep amboceptor.
Tabes	+	×	3 units natural amboceptor.
Periostitis, specific	+	—	2 units natural amboceptor.
Stricture rectum	+	—	Natural amboceptor.
Epiphysitis, specific	×	—	
Endometritis (abortions)	+	=	Wassermann suspicious.
Osteomyelitis, specific	+	×	Na natural amboceptor; goes negative on addition of two units artificial amboceptor.
Chronic endocarditis, nephritis	×	—	4 units natural amboceptor present.
Diabetis insipidus	×	—	Excess amboceptor.
Hodgkin's disease	+	—	Chancre about 20 years ago.
Proctitis	×	—	Under Hg treatment till recently.
Ulcus cruris	+	—	Chancre 25-30 years ago.
Spastic paraplegia	×	—	Spinal fluid negative.

+, Positive. —, Negative. ×, Weakly positive to moderate. =, Only suspicious.

Non-Syphilitic Conditions.—As mentioned already the value of the test depends upon its specificity. No method is of any diagnostic value, if the test gives a positive reaction in ordinary non-syphilitic diseases. Of course it is now a well-established fact that the Wassermann reaction is not a specific test for syphilis alone, as it usually gives positive reaction in mixed and tubercular forms of leprosy, and in yaws. It also gives a positive reaction in certain protozoal diseases, such as malaria and sleeping sickness. In malignant tumors and scarlet fever the Wassermann reaction was found to give occasional positive reaction, even in the hands of certain

workers. However, this is very rare. In this respect my method is not any different from the original, but it differs from all other modifications using active human sera in not giving a non-specific reaction as frequently as the latter do; a fact due to the difference in the antigen preparations. I am absolutely convinced that there is no danger of getting non-specific positive reaction with active sera so long as one uses protein-free aceton-insoluble lipoids selected by my standardization. That this conviction has been amply confirmed by other investigators may be seen from the following table:—

TABLE IV.

		+	—
Noguchi	1642	....	....
Kaliski	750	....	....
Jeffries und Pease	300	....	....
Schwartz	250	....	....
Robinson (Orleman)	250	....	....
Lederer	150	....	....
Fox	113	....	....
Groat	125	....	....
Corson-White	183	....	....
Craig	214	....	....
Potter (Alfred)	45	....	....
Schradieck	100	....	....
Waugh	30	....	....
	4152	0	4152

Some of the investigators have obtained positive reactions in certain non-syphilitic cases, among which leprosy is the principal disease. I refer the reader to the excellent work of Fox, who studied nearly 60 cases of leprosy with my method. In malaria, Craig obtained a positive reaction in the febrile stage of the disease, but a more extensive study of this disease seems desirable. Pellagra was once reported by Bass (using the Wassermann system) to give positive reactions in a large percentage of cases, but Fox and Litteras failed to confirm Bass's findings, having obtained negative results in nearly 50 cases examined by my method, as well as by the Wassermann.

Kaliski examined a very large number of patients at the Mount Sinai Hospital of New York, going from ward to ward without previous knowledge of the cases. He obtained the results upon which he based the following conclusions:—

As a result of more than a year's experience in the performance of the Noguchi and other systems of complement fixation-tests for syphilis, during which time I have examined more than a thousand specimens of blood, I am of the opinion that the claims of the originator of the anti-human system are well-founded.

The method is simple and easily carried out.

The reagents for use in the test can be prepared in stable form in cen-

tral laboratories, thus putting the test within the reach of some workers who would otherwise be compelled to do without this means of diagnosis.

A comparison of the Wassermann and Noguchi systems shows that the latter is at least as sensitive as the former in the earlier stages of syphilis, while in the later stages, in treated syphilis and in the so-called metasyphilitic conditions, it is more sensitive.

The Noguchi system is specific. Either active or inactivated serum can be used provided the essential technical procedures are carefully followed. A positive reaction therefore can be interpreted as evidence of syphilis with the same degree of assurance as applies to the regular Wassermann test.

The work of Pedersen, Orleman, Robinson, Craig, Waugh, Groat, Schradieck, and others in dermatology and genito-urinary conditions, of Moore, Rosanoff, Wiseman, Atwood, Kaplan, Corson-White, and others in psychiatry and neurology, of Martin Cohen and Bulson in ophthalmology, of Fowler in otology, shows conclusively that the method introduced by me gives a reliable and uniform result in the hands of those who mastered the technique thoroughly.

Conclusions.

1. The complement fixation-test for syphilis by the method introduced and developed by me is specific in the same degree as is the Wassermann method. It is somewhat more sensitive than the Wassermann in syphilis and parasyphilis, but is not too sensitive as to endanger the diagnostic value of the test.

2. My method is especially suitable in following the effects of antisyphilitic treatment on account of its delicacy.

3. My method is strictly quantitative in construction, having every factor entering the reaction under quantitative control. By this method the estimation of the strength of the positive reaction can be made in an accurate way. The Wassermann method is defective in this special point, as no quantitative work is possible with that method.

4. The quantity of the blood required for my method is nearly one-tenth of that needed for the Wassermann. The time and labor for carrying out my method is very much less than for the Wassermann.

5. The preparation of the necessary reagents and performance of the test may be separated and done by two different sets of workers. The performer of the test is not required to be capable of preparing the reagents in order to get reliable results, while in the Wassermann method the performer must be capable of preparing the reagents before his results are to be trusted.

6. The most essential and difficult reagents for the test are made stable in my method, while this is not yet accomplished for the Wassermann

method. The adherents of the latter still follow the formula in detail laid out by Wassermann several years ago, hence their reagents are in a most unreliable state.

7. From the foregoing it is a benefit for every physician to specify which method he desires to be employed for examination of his specimens. The two methods are not equivalent in yielding the exact results.

ON THE MEANS OF FINDING THE SPIROCHÆTÆ PALLIDA WITH SPECIAL REFERENCE TO THE INDIA INK METHOD.*

By J. S. Cohn, M. D., of Chicago.

The large number of investigations which have recently been made upon the etiology of syphilis practically all started with the discovery of Schaudinn and Hoffmann in 1905,[1] of the treponema pallida. The importance of this discovery and of the subsequent work proving the etiological relation between this spirillum and syphilis has been great, and it was only through the establishment of lues as a spirillosis that the therapeutic endeavors of Ehrlich have been possible. As is well known now, Ehrlich's first studies were made on animals infected with spirilla, and later extended to syphilis in animals and men. Before the treponema pallida was identified as the cause of syphilis, the disease was a clinical entity, the diagnosis depending mainly upon the symptoms, the important ones of which appeared in the secondary stage some time after infection occurred. Vigorous treatment then could not be instituted until the diagnosis was made, i. e., in the secondary stage, as it would be unsatisfactory, if not unjustifiable, to submit a patient to a two years' mercurial treatment for a suspicious non-specific lesion which resembled lues. On the other hand, if the lesion were specific, by the time the secondaries appeared, the system would be so saturated with the causative agent, that treatment was at a disadvantage. Now that the etiological factor is identified, and the treatment is at hand, the latter can be instituted at once, providing the diagnosis is made. This practically depends upon finding the spirochætæ pallida in the various lesions present.

The evidence that the spirochæta pallida is the cause of syphilis can be summed up as follows: First, the almost constant demonstration of the spirochæta pallida in the products of the various syphilitic lesions; second, the finding of these organisms in the organs of fetuses and infants inheriting active forms of syphilis; and third, the transmissibility of the syphilitic virus to the lower and higher monkeys and to the eyes of rabbits, guinea-pigs and dogs, and the recovery of the spirochætæ from the lesions produced. Although the cultivation of the organism on artificial media is a matter of considerable difficulty, objection on this ground to its being the etiological agent is no more justified than doubt that the plasmodium malariæ causes malaria. The treponemæ pallida

*From the laboratories of the Michael Reese Hospital, Chicago.

are found constantly in all chancres and the regional glands and in all condylomata and mucous patches. In these they are far more numerous than in any other lesion, which corroborates the former evidence that the disease is especially communicable through lesions of this nature. They may be demonstrated in other secondary lesions such as the papillary syphilide and less often in the tertiary lesions; and are also found in the placenta and fetal organs of still births due to lues. Noeggerath and Staehelin[2] claim to have found them in the circulating blood.

These organisms are found both in smear and tissue preparations. In smears, they are found by staining, by the dark field illuminator and by the India ink method. As the same material is employed in the above three methods, it is well here to describe the manner of obtaining it. The lesion which can be any of those mentioned above is first cleansed if necessary with soap and water to remove any pus or granular epithelial debris. Sometimes the irritation produced by the gauze alone on an ulcerated surface will bring forth numerous bleeding points. At other times the surface of the lesion, especially a mucous patch or papule, must be curetted with a small scalpel or other sharp edged instrument, until the flow of serum is produced. The lesion should be curetted where the sound and necrotic tissue join, and sometimes the floor of the lesion must be scraped. As only serum is desired, any blood is wiped away, and the eroded surface compressed firmly with gauze. This checks the hemorrhage, and immediately upon removal of the gauze there is a copious flow of serum from which a drop or two can be taken for smears. The serum should exude from the living tissue, as the spirochæta pallida is a true parasite and lives in the tissue, whereas the spirochæta refringens is only a surface grower.

The serum should be spread on the slide in a thin film. Of the stains several have been employed, the results of which show that the anilin dyes impregnate the protoplasm of the spirochætæ pallida to but a slight degree and that solutions containing eosin and azure blue will stain the pallida more intensely. It is upon the latter fact that the Giemsa stain depends. This stain was first used by Schaudinn and Hoffmann (l. c.), but since then various modifications have been employed with the object of lessening the time for the staining reaction which was always a disadvantage, being from eighteen to twenty-four hours in duration. Practically all the modifications are of equal value, so only one will be described here.

Schereschewsky's[3] method is very simple and has met with considerable success. The slides are air dried and passed through the flame three times. The staining mixture is freshly prepared by adding 13 drops of Giemsa's solution (Grueblers) to 10 c.c. of a 0.5 per cent. watery glcerine solution. The mixture is heated to boiling and poured on the slide for three to five minutes. It is then poured off, the slide washed in neutral distilled water, dried rapidly in air and a second application

of the stain then made. A third and fourth are made if necessary. The treponemæ stain deep pink with the background pale in comparison. In the above method it is important that the slide or coverglass be free from grease and that the test tube and slide forceps should be clean, free from acid and any precipitated stain.

Various modifications of the original polychrome methylene blue-eosin stain of Romanowski have been adapted for staining the spirochætæ pallida but not generally used. Geraghty[4] has employed Hasting's stain with excellent results. The smears are dried in the air and covered with the stain for one minute. Then distilled water is added until a metallic lustre appears, and the smear is stained for five minutes more. They are then washed in running water, dried and examined. The pallida stain faint blue with a pinkish tint and the refringens a deep blue.

Stern's[5] silver method for smear preparations stains the spirochætæ pallida intensely black, but it causes a swelling of the cell body and they do not appear as delicate as they are. It is as follows: Dry the smear in air and place in the incubator at 38° C. for several hours, then in a 10 per cent. solution of silver nitrate in a colorless glass container which is allowed to remain in diffuse daylight for some hours until the film appears brown with a metallic lustre. Better results are obtained by exposure to weak diffuse daylight for three to five days.

The dark ground illuminator is certainly effective for rapid diagnosis and one has the advantage of seeing the organism in the living state, observing its various movements and manner of reproduction, but owing to the nature of the apparatus required, its employment is rather limited. As the spirochætæ are poorly refracting bodies, they shine through as light areas upon a dark background.

The reason special reference is laid upon the India Ink method, is because of its extreme simplicity and the fact that anyone with even a moderate knowledge of the microscope can have within his reach a rapid microscopic diagnosis of syphilis. Burri[6] in 1909, noticed that bacteria were not stained by India Ink and that their presence in thin smears left clear spaces. Hecht and Wilenko[7] in the same year, published their observations that the treponema pallida was easy to identify by this method, and Fruehwald[8] later published his very complete article on this method of finding the treponema. Serum is produced from the lesions as for the above smear preparations. One loopful of serum is mixed with one loopful of India ink on a glass slide and the mixture is immediately spread over the slide in a thin film by drawing the edge of another slide over the first, as in making a blood smear. The film dries in half a minute without heat and should be dark brown to black in color. It is placed at once without mounting or further fixation under the oil immersion lens. On examination, the whole field is seen to be of a homogeneous brown or black color, with the spirochætæ, blood-cells, and other extraneous material shining through as colorless refractive bodies. When present in

moderate numbers, they are usually observed in a very short period of time. The glass slides should be perfectly clean so that the India Ink will adhere. By this method, the refringens and other spirilla are also readily found, and occasionally one may find both the pallida and refringens in the same preparation. So simple is this method that we have found spirochætæ pallida under the microscope three minutes after first seeing the patient. There are practically no drawbacks to this method, except in the use of certain preparations of ink in which too many granules are present. The best ink to employ is the Chin-Chin liquid pearl ink, manufactured by Gunther-Wagner, though fair results may be obtained by other inks, such as Carter's or Higgin's.

The recognition of the spirochætæ pallida depends upon the observer's ability to differentiate them from other spirillæ and to appreciate their distinct morphological characteristics. In size it varies in length from 7 to 21 microns, *i. e.*, about one to three times the diameter of a red corpuscle. This comparison is beautifully shown by both the dark ground illuminator and the India Ink method. Longer forms are sometimes seen, but they are probably two or more organisms. It has the shape of an extremely slender thread, closely wound in a cork screw form, the windings being very acute and absolutely regular. When seen with the dark ground illuminator, they are observed to rotate on their long axis in either direction. The motion is very rapid but not necessarily accompanied by a change of position. They progress from place to place but not so rapidly as most other forms of spirichæta, and they have a quick and spasmotic bending or twisting motion, which increases as the specimen grows older.

A careful microscopical examination renders the differentiation of the treponema from all other spirilla certain. The majority of these on account of their coarser form, their irregular and broader convolutions and their greater affinity for stains, can scarcely be confused with the spirochætæ of syphilis. The spirochæta refringens is very readily differentiated as it has no points in common, and when once seen along side of the treponema pallidum it can never be mistaken. Its thread is thicker, it has but four or five convolutions which are much broader than those of the pallida and of a more wavy form. It is a surface grower and is found in suspicious lesions. The spirochætæ buccalis and dentata both have thicker threads which are wider than the pallida and have fewer and less angular convolutions. These are found in unclean mouths and teeth. Vincent's spirillum resembles very closely the spirochæta refringens, but as it is always associated with the fusiform bacillus, it should cause no confusion, especially when making smears from lesions on the tonsils.

In summarizing the literature of the last five years on this subject, it is evident that most workers agree that the spirochæta pallida is the cause of syphilis. The methods of demonstrating the organisms have passed through the long and tedious Giemsa stain to the extreme sim-

plicity of the India Ink. Schaudinn and Hoffmann (l. c.), Schereschewsky (l. c.), Geraghty (l. c.), White and Avery,[9] and numerous others report excellent results with the Giemsa stain or with its modifications. No one doubts the efficacy of the Levaditi method for demonstrating the spirochætæ pallida in tissue sections. The dark ground illuminator is by all means the most efficacious, showing the living organism and permitting the study of fresh untreated material. The India ink method has met with considerable favor wherever it has been tried. Barach[10] recently criticised this method on the ground that the ink itself contains substances sufficiently similar to the spirochætæ pallida to confuse one who is not an expert microscopist. This criticism referred especially to the Higgins ink, but he also found similar wavy bodies in various other inks tested, including the Gunther-Wagner, the use of which has been generally advocated. In numerous observations totalling about four hundred, we have never found in smears made with the Gunther-Wagner ink, any artefacts resembling the spirochætæ pallida. These organisms, when once seen, leave such a vivid and definite impression that it is impossible to confuse them with anything else. Higgins and Carter's ink, we have never used as a routine procedure, as they are too granular, but we have made many smears of both inks, and in none of them was anything resembling a spirochæta seen. Indistinct wavy detritus may be seen, but it does not resemble the pallida.

Our personal experiences have been limited practically entirely to India ink. Early in our work it was found that pictures obtained by this method and by the various stains, could not be compared in definiteness. The very numerous examinations to be made, rendered the routine use of the dark field illuminator difficult.

Through the kindness of Dr. Jobling, we were given the opportunity of studying the cases of syphilis treated at the Michæl Reese Hospital, with Ehrlich's "606." We were able to examine lesions of all sorts, especially chancres, mucous patches and secondary skin lesions, both before and after injection. All told approximately four hundred examinations were made. In every case except those which had been previously submitted to a long mercurial treatment, the spirochætæ were easily and quickly found. It should be emphasized here as a safe rule to follow, that if any doubt exists that an organism is the spirochæta pallida or not, one should without hesitation, give a negative report. We cannot state too strongly that the picture presented by the India ink method, is absolutely sharp. The gradual disappearance of the organisms following injection of comparatively small doses of "606," was in striking contrast to the rapid disappearance following larger doses.

How valuable the India ink method is for the demonstration of the spirochætæ pallida in scrapings made from syphiltic tissue, such as fetal liver or placenta, still remains in some doubt. Our experience has not been very extended or conclusive, as at times we have found them in the

tissue and at other times we have been unable to demonstrate them even when later studies with the Levaditi stain showed their presence. It seems to us, that with the proper maceration and extraction of tissue, one should be able to obtain a homogeneous mixture with India ink, permitting its use here instead of the long Levaditi stain, and at present we are attempting to demonstrate the feasibility of this procedure.

In conclusion, I wish to thank Dr. J. W. Jobling, for permission to make this report, and Dr. S. Strouse, for assistance in its preparation.

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THE HISTORY AND METHODS OF APPLICATION OF EHRLICH'S DIOXYDIAMIDOARSENOBENZOL.

By Lewis Hart Marks, M. D.,* of Frankfort, Germany,
Member of the Royal Institute for Experimental Therapeutics, Frankfort o/M.

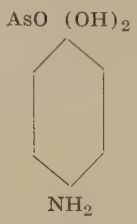
For many years before Paul Ehrlich was able to achieve his purpose, it had been his desire to enlarge the scope of the hitherto accepted principles and limitations of pharmacology. He was not satisfied merely to determine the toxicity of different drugs, and their effects upon the circulation and the various organs of healthy animals; or to leave unanswered the main therapeutic question—namely, how drugs really act upon the causative factors of parasitic diseases. In 1905 the opportunity he had so long been waiting for was given him, by the founding of an institute in the city of Frankfort, devoted exclusively to the carrying out of his ideas. Here was started the new science of Specific Chemical Therapy, or Biological Therapeutics. He set to work to make many new drugs: drugs that would be specifics for one particular parasite and above all to study how these drugs were distributed through the body and how they acted upon the parasites themselves. He conducted these studies not upon healthy animals but upon animals infected with a particular parasite. Sleeping sickness, or better the trypanosome, was selected as the first parasite which should be studied.

Béchamp's incorrect formula for Atoxyl.

Atoxyl was brought into prominence in medicine first by Thomas in the Liverpool School of Tropical Medecine, and, as it proved to be a drug possessing great trypanocidal properties, it was then used by Kopke on sleeping-sickness patients in Africa. As this drug fitted into Ehrlich's plans, he started to study the drug itself and its properties. It was first discovered by Béchamp, a French chemist, in 1863, who believed it to be a very loose combination of analin and arsenic acid; in other words, that a molecule of nitrogen intervened between the arsenic-acid group, and the benzol ring of the analin.

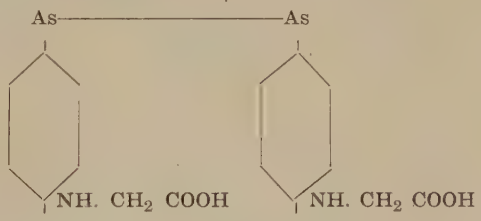
*The author's prolonged stay abroad has been made possible by a grant from the Rockefeller Institute for Medical Research, New York.

Ehrlich soon discovered,—and the same thing was soon thereafter discovered independently by Prof. Puckner, in the laboratory of the American Medical Association,—that the product was a very stable one, contrary to Béchamp, and that the arsenic-acid group was connected directly with the benzol ring of the anilin, and that the amido radical was



Ehrlich's (the correct) formula for Atoxyl.

in the para-position to the arsenic-acid group. This discovery showed that the product was capable of withstanding many different kinds of chemical manipulation, and many different substitution products could be made from it. The history of dioxydiamidoarsenobenzol can be said to have had its origin in this discovery, as it is but a modification of one of the main reduction products of atoxyl. In changing this substance by the introduction or removal of certain radicals, it was found that it could be made more or less toxic at the will of the chemist.

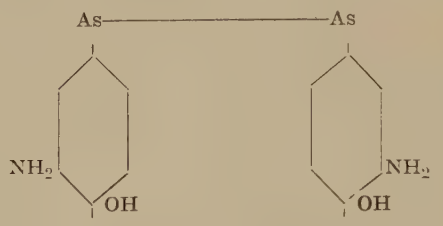


Formula of Arsenophlenylglycin.

Ehrlich had also previously found that trypanred, a dye-stuff which had no effect whatever upon the trypanosomes when mixed with them in a test-tube, possessed, on the other hand, great trypanocidal properperties within the body. He explained this paradoxical action by assuming that the trypanred was reduced within the body into a trypanocidal substance. This explanation was verified by his experience with atoxyl and its substitution products. He found that the reduction products which he made outside the body were more active in the body, proportionally to the amount of their reduction. So products were made more and more reduced (and these were then further modified) until one was found, the 418th—Arsenophenylglycin—which in one injection cured all animals even in the last stages of trypanosomiasis. This drug was then turned over to the workers in Africa, and Ehrlich began his study of syphilis.

This arsenophenylglycin contains arsenic in the reduced state, that is threevalent arsenic, and is a double combination, known as the arseno combination.

By removing the incomplete acetic-acid radical from its combination with the amido radical, and introducing a hydroxyl radical in the para-position to the arsenic-acid group and placing the amido group in the ortho-position we have 606.



Formula of Dioxydiamidoarsenobenzol (606).

The substance was first tried on chickens infected with spirillosis and on mice infected with the spirillum of relapsing fever. Hata soon found that one-fifty-eighth of the *dosis tolerata* would suffice to cure a heavily infected chicken, and also that a very much smaller dose than the *dosis tolerata* was required to cure a mouse of relapsing fever. He next studied the effect of this drug on syphilis working with rabbits. The rabbit is infected by introducing under the skin of the scrotum a small portion either of condyloma from a human being, or better, as it is done in the laboratory, from the testicular chancre of a previously infected rabbit. In a few weeks a typical chancre develops, which if allowed to run on, involves the entire scrotum. In these lesions the spirochætæ pallida exist superabundantly. Hata found that one-seventh of the *dosis tolerata* was sufficient to cause all the spirochætæ to disappear entirely from these lesions within forty-eight hours, and to cause complete healing of the ulceration in a few weeks. The next step was to start treating human beings, which was most difficult. Very few men could be found who were willing to be the first to be injected with such a powerful and unknown drug. In Prof. Conrad Alt of Uchtspringe, Ehrlich found both a willing and more than satisfying helper. Alt had previously had experience in injecting paralytics with arsenophenylglycin, which he had done in the most careful and painstaking manner. In this same way he undertook to introduce the treatment of human beings with "606." First he studied the effect of "606" upon dogs, and its excretion from the body. Then two of his assistants volunteered to have themselves injected with the drug, which was then not yet so perfected as it is now, and the solution was very strongly alkaline. They paid for their heroism with many days of the most severe pain. As the drug did not produce any other unsatisfactory symptoms, its introduction into human therapy was inaugurated. Since then much has been written and more has been said

about it, and a great deal of experience has been gained. Many methods have been suggested, tried, and after a longer or shorter period of time, have been found wanting in some particular, and discarded. Strange to say, our experience has taught us, that the original methods, advised at first by Ehrlich, are still the best and are the ones that should be used.

The technique of injecting "606" must be divided into two main heads: First, the intramuscular injection of the clear alkaline solution; and, second, the intravenous injection of the alkaline solution either by the method of Schreiber or Weintraud.

The results obtained have forced Ehrlich strongly to recommend, that the neutral suspension method of Wechselmann, Michaelis and Blaschko, and the injection of the sterile liquid paraffine suspension, as suggested by Kromayer, be abandoned. Unfortunately the clear alkaline solution causes considerable pain in many cases, but if it rapidly brings about the disappearance of longstanding lesions, which other drugs have failed to affect, this disagreeable, merely temporary, effect should certainly be overlooked. The alkaline solution is prepared in the following manner: Into a thin, 25 c.c. graduated cylinder with a ground glass stopper about

FIG. I.

two dozen small glass beads are put. The stopper is then inserted and the whole is then sterilized in dry heat. In order to avoid repetition it must here *emphatically be stated,* that all the apparatus used in the injection and the hands of the operator, as well as the field of injection, must be *thoroughly sterilized,* since many of the bad results that have been reported have been due to carelessness in this direction.

Nine c.c. of hot distilled water are now poured into the graduated cylinder and the mouth of the cylinder is then dried with a piece of sterile gauze, to prevent the substance from sticking to it. The tube containing the substance after having been washed in alcohol and ether is opened by means of a glass cutter and the substance poured into the cylinder, which is now closed with the glass stopper and well shaken for about one to two minutes when the substance will be found to be completely dissolved. From a drop-bottle a 15 per cent. solution of sodium hydrate is added drop by drop to the solution in the cylinder which is thoroughly shaken between each drop. After a few drops have been added to the solution the substance will start to precipitate, and this will continue until sufficient sodium hydrate solution has been added to cause

the substance to redissolve. The clear alkaline solution is then ready to be injected. Care must be taken to shake the contents of the cylinder well between each drop of the sodium hydroxyde solution, as in this way the clear solution will be obtained with the smallest possible quantity of the alkaline solution, and the less there is of the latter the less pain is produced. Various substances have been added to this solution to lessen the pain, but, as the greatest pain appears on the second or third day, these have very little effect. The writer has found that 1 c.c. of a 2 per cent. carbolic acid solution, if added to the solution and mixed well with it just before injecting, prevents a great deal both of the immediate and later pain. The 9 or 10 c.c. composing the finished solution should be injected as quickly as possible, after the preparation has been made, deep into the gluteal muscle either on one or, divided, into both buttocks. The dose used for the intragluteal method is about 0.08 c.c.

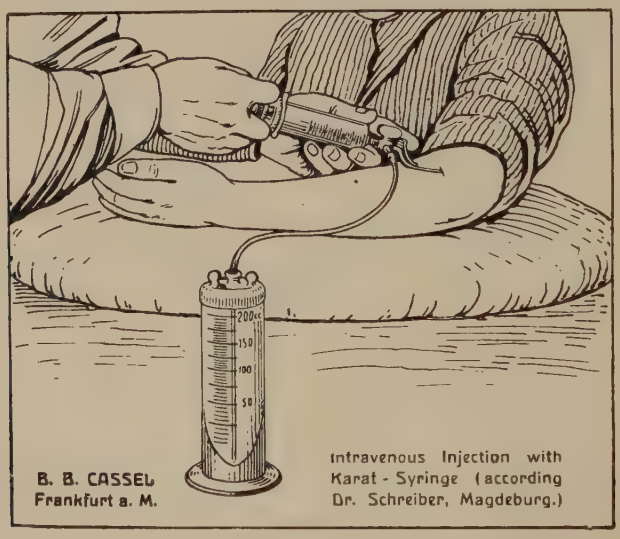


FIG. II.

As to the Intravenous Methods.—Schreiber's method* is carried out as follows:—The special needle used (Fig. I.) is in the form of a bayonet and is fitted with a three-way-cock which allows the solution to be drawn up into the syringe through a rubber tube from the special graduate, and a simple turn of the cock allows the injection of the fluid into the vein. The cock is again turned and the fluid is again drawn up into the syringe and more is then injected into the vein; this process being kept up until the desired quantity has been infused. Of course the needle must first of all be securely placed in the vein (Fig. 2), which is made easier by cutting off the venous circulation in the arm, by fastening a rubber tube

*Schreiber: *Muenchener Medizinische Wochenschrift*, No. 39, 1910.

around the arm until the cubital vein swells sufficiently to allow the insertion of the needle, when the rubber tube is loosened. Schreiber prepares his solution in the following way:—

In a graduated cylinder holding 250 c.c. with a small neck and a ground glass stopper he puts 10 to 20 c.c. of hot water. Then he pours in the substance and shakes the solution until the substance is completely dissolved. Sufficient warm, sterile water or physiological salt solution is added to bring the quantity up to 100 c.c. Then for every 0.1 of substance he adds about 0.7 of normal sodium hydroxide solution. The whole is then well shaken until the resulting precipitate redissolves. If this resolution is not complete after thorough shaking, a few drops of the alkaline solution are added, and this is continued if necessary, until an absolutely clear solution is obtained. Salt solution is then added up to the 200 c.c. mark. The solution is then poured over into Schreiber's special glass, and is then ready for infusion.

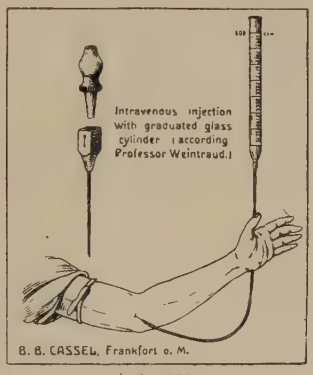


FIG. III.

Special care must be taken with this method not to inject any air into the vein.

The Weintraud* method is simpler and preferred by the writer. Here a special needle (Fig. 3), but a simpler one is also used, which the figure sufficiently explains. The solution is prepared as follows:—The substance is placed in a short broad cylinder in which 30 to 40 c.c. of hot sterile water have previously been poured. The substance is assisted to dissolve by rubbing it against the walls of the cylinder with a glass rod. When the solution of the drug is complete it is poured into a flask containing 200 c.c. of warm physiological salt solution. One-fifth normal sodium hydroxide solution is now added in small quantities, until the substance precipitates and again completely dissolves. This requires about 20 c.c. for 0.5 grm. of 606. Here also an excess of the sodium solution is to be avoided, and this can best be done by shaking well the flask containing the solution after each few drops of the sodium hydroxide

*Weintraud: *Medizinische Klinik*, No. 43, p. 1683, October, 1910.

solution are added. The clear solution is then poured into the long glass cylinder (Fig. 3), all the air being expelled by an assistant who also controls the flow of the fluid. The front part of the needle is inserted into the vein as described above, the blood is allowed to flow, the constriction above is removed, and the rear part of the needle which is attached to the rubber tubing is then inserted, care being taken that an inrush of air with the first flow of the fluid is prevented. Both Weintraud and Schreiber advise simply dressing the puncture with a piece of adhesive plaster immediately after the removal of the needle.

The advantage of the intravenous method is that very little discomfort is caused the patient at the time of the injection—only the needle-prick is felt—and no pain is felt at all thereafter. And the substance is brought immediately and in the greatest possible concentration into direct contact with the parasite. These are the reasons why Ehrlich now recommends the general use of the intravenous method.

General Remarks.—Because of the confusion in the available statistics and because of the smallness of the dose that is being used, it is almost impossible to ascertain at the present time, what percentage of patients can be completely cured with one injection of the drug. We know, however, that many recurrences have occurred, and as the specific action of the drug upon the spirochætæ has absolutely been demonstrated we should now try our utmost definitely to cure our patients. If at some future date it is found that a much larger dose given in the alkaline solution, intramuscularly, is sufficient completely to conquer the disease, then we would be justified in abandoning Ehrlich's present attitude. This will surely be the case, as the *dosis tolerata* for a human being computed from the average *dosis tolerata* for all animals would be 5 to 7 grm. At present Ehrlich regards the matter as follows:—He says, a patient should be injected intravenously (0.4 to 0.5 grm. for women, 0.5 to 0.6 grm. for men), and this injection should be repeated from three to eight days after the first injection. If at the end of four weeks the Wassermann reaction is still positive another injection should be made. There is absolutely no danger in frequently repeating the intravenous infusion of "606" from the standpoint of hypersusceptibility. On the contrary, it appears that the patient stands the second injection better than the first.

In Conclusion a Word of Warning.—About the time of the appearance of this article, "606" will be put into the hands of the profession at large. It must always be remembered that it is a most powerful medicinal agent, and the greatest care must be observed in using it. Only those specially trained should use it, or else they will suffer grave disappointments. During the first six months of its general use it will surely be exploited by the unreliable and its real value will frequently be questioned. Only after it has passed through this stage and become concentrated in the hands of the capable will its worth be recognized and Paul Ehrlich's latest discovery be given the place that it truly deserves.

SYPHILIS OF THE NERVOUS SYSTEM.

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With the exception of parasyphilitic diseases, which have separately to be considered, syphilis produces in the nervous system pathological lesions exactly akin to those produced elsewhere in the body; the special features of syphilis of the nervous system therefore altogether depend on the physiological peculiarities of this system. The variability of syphilitic lesions and the complexity of neurological symptomatology combine in making the subject of the present paper an extraordinarily extensive one, a fact well illustrated by the richness of the latest monographs on the subject.* It will obviously be possible here only to select from it a few general considerations or special points of particular interest to the practising physician.

The chief lesions produced by syphilis may histologically be enumerated as follows: primary toxic degeneration, small-celled infiltration, and reactive proliferation of connective tissue-elements. In a given case any one of these may be not only more prominent than the others, but may constitute the chief feature; this influences not only the clinical course run by the condition, but also the symptomatology. The second type of lesion is apt to cause acute affections which in a short time recover, either partly or completely; the other two lead to more chronic states, which are also on the whole distinctly less amenable to treatment. Added sources of complexity in the clinical picture are due to the facts that syphilitic lesions are most often numerous and irregularly distributed, and that in a given case different forms of lesion may either coexist or succeed one another. Variability and irregularity are thus features of the affection that are important from a diagnostic point of view; they are rarely met with in the same degree in any other nervous disease with the exception of disseminate sclerosis.

It has further to be remembered that syphilis may affect the nervous system in indirect ways, the most obvious of which is through affections of the cerebral blood-vessels or of other neighbouring structures, such as the enclosing bony cases. Neuroses may be causally related to syphilis in a variety of ways: first through the bodily exhaustion due to severe

*Mott: Syphilis of the Nervous System, 1910; Nonne: Syphilis und Nervensystem, 2 Aufl., 1908. Of the two the former is perhaps the better on the pathological side, the latter on the clinical.

general syphilis, secondly through the mental impression produced on sensitive subjects by the idea of having contracted what is popularly thought of as a loathesome and guilty complaint, not to speak of various possible domestic complications, and thirdly, in the absence of the disease, through the haunting dread of infection known as syphilophobia.

It will be most convenient to consider the various effects of syphilis on the nervous system in the order of the lesions mentioned above. One form of primary degeneration of the nervous tissue, which has given rise to much discussion and investigation, is that described by Erb in 1892 under the name of "syphilitic spinal paralysis." The spinal cord is more or less implicated in the majority of cases of syphilis of the nervous system, usually by a number of local lesions, but Erb maintained that occasionally the disease affects the cord alone, and in a peculiar way, namely by causing a diffuse degeneration, principally of the pyramidal tracts. The symptoms then are those characteristic of spastic paraplegia, from the pure type of which it differs, however, in the presence of slight sensory disturbances, with paræsthesias, in the early occurrence of bladder troubles, and in the rigidity being less pronounced than might be expected from the amount of increase in the deep reflexes and from the markedly spastic gait. At least half a dozen autopsies of this condition have been made; the degeneration found is not confined to the pyramidal tracts, but is diffusely distributed, implicating particularly the posterior columns as well; strictly speaking, it is not a systemic degeneration such as is found in amyotrophic lateral sclerosis and other diseases. The prognosis is generally, though not uniformly, bad, and at any time the case may be complicated by the occurrence of other syphilitic disease.

Another condition in which primary toxic degeneration plays a large part is a certain type of idiocy. Recent investigations by Plaut, Dean and others have shown that the Wassermann reaction is present in the blood in more cases of idiocy than might previously have been suspected. It is not yet definitely known what proportion of cases of ordinary idiocy is due to congenital syphilis, but it is certainly a considerable one, possibly amounting to twenty per cent; the Wassermann reaction may be found even when no other signs of congenital syphilis are evident, just as it may in adult cases of parasyphilis.

The second type of lesion is the most frequent. There is no part of the nervous system, and no form of tissue contained therein, that it may not affect. In the great majority of cases both the brain and the spinal cord are affected, but in most of them the lesions predominate in one of the two. Of the two the brain is more often affected. Usually, as was mentioned above, one finds a combination of different types of lesion; thus it is very common to find syphilitic changes in the cerebral arteries, with the mechanical consequences of these (softening, etc.), at the same time as numerous gummatous formations, or a more or less diffusely distributed infiltrative process.

The peripheral nerves may be affected by syphilis in several indirect ways, for instance by pressure or extension from lesions in neighbouring structures, glands, bones, etc. Up to the present it cannot be regarded as proved that syphilis may produce a primary, parenchymatous, peripheral neuritis, either local or general. In cases where the symptoms point to the diagnosis of neuritis it will usually be found that local infiltrative or proliferative lesions are present. Perhaps the most frequent affection in this group is the so-called syphilitic root-neuritis. The spinal nerve-roots may become affected in a variety of ways: they are sometimes pressed on by a pia that is inflammatorily thickened, they may become secondarily infiltrated by an inflammatory process beginning either in the pia or in the blood vessels, changes in the vessels may induce secondary atrophy of the nerve-roots, and finally gummata may begin here as well as elsewhere. One never finds any of these lesions without finding coexistent ones in the spinal cord as well. It is disputed whether syphilis can cause true neuralgia or migraine apart from the usual gross local changes, but it is not probable.

The symptoms of syphilitic affections of the cord are those of cord affections in general, and the special features reside rather in the distribution and course than in any characteristic group of symptoms. Thus, to take a single example, paraplegia may be produced by gummata growing from the vertebral periosteum, from the meninges, or in the substance of the cord, by vascular disease, by a meningo-myelitis, a focal chronic myelitis or an acute transverse myelitis. Evidently the features of the paraplegia will vary according to whether the lesion is local or diffuse, single or multiple, intra-medullary or extra-medullary. There is hardly any spinal cord disease that may not be mimicked by syphilitic affections; the typical clinical pictures of syringo-myelia, of anterior poliomyelitis, of Landry's disease, of cerebro-spinal meningitis, a Brown-Séquard syndrome, may all be produced by syphilis alone, facts often not realized, and of obvious importance for diagnosis. Much attention has been paid in recent years to the frequency with which a mild form of meningitis occurs during the secondary stage of the disease; the symptoms due to this, lumbar pain, paræsthesias and weakness of the limbs, slight irritability of the bladder, and increased activity of the deep reflexes, had long been recognized as being typical of "meningeal irritation," but the findings of lumbar puncture have shown that there is present an actual inflammation of the meninges.

The prognosis of most syphilitic affections of the cord is a serious one, perhaps more so than is generally thought. In some forms it is almost hopeless; the acute transverse myelitis, for instance, is usually rapidly fatal. It is always wise to give a guarded opinion concerning the future, for even cases that apparently recover are often found to suffer from later troubles, when they are watched over a number of years.

Disease of the arteries plays an important part in the spinal affections,

but it is rarely so predominant as it is in many of the cerebral cases, where it may constitute the principal lesion. The results of syphilitic disease of the cerebral arteries are the same as those of any other diseases of these, and can be distinguished from them only by collateral evidence. The commonest are those due to partial or total occlusion; it is characteristic for these to be for some time of a prodromal nature, due to the former condition, such as diffuse, boring headache, spells of faintness, transitory attacks of weakness or numbness in one or more limbs, etc. Total occlusion, with thrombosis, leads to the usual consequences of this, which vary according to the rate of onset, site and extent of it. As throughout is the case with syphilitic affections of the nervous system, transitory manifestations, partial effects, and irregular recurrences, are common. For instance a temporary paresis of one limb may occur, to be followed by a slight aphasia, and then perhaps by a total hemiplegia or triplegia. Cerebral hæmorrhage is a far rarer effect of syphilitic arterial disease than thrombosis, though it sometimes occurs, particularly after the formation of aneurisms in the larger vessels. In ordinary cerebral hæmorrhage, due to atheromatous changes with or without the formation of miliary aneurisms, it is probable that syphilis is only occasionally the pathogenic factor.

Chronic syphilitic meningitis over the convexity of the brain is, perhaps more than any other syphilitic affection, marked by variation between progressive and retrogressive changes, with a corresponding fluctuation in the symptoms. The lesions are more pronounced in the dura, whereas those of basal syphilis are more pronounced in the pia. The most constant symptom is the characteristic form of headache. Others, in the order of their frequency, are: giddiness, vomiting, mental changes, pupillary alterations, epileptiform attacks with or without paralyses, and, more rarely, choked disc, sensory disturbances of the cortical type, speech anomalies, and hemianopsia. They are throughout, therefore, the symptoms of irritation of different areas of the cortex. The epileptiform attacks may present any type from the well-known Jacksonian one to the general attacks of "idiopathic" epilepsy; they are frequently followed by a temporary paresis of one or more limbs. It is important to bear in mind that sometimes the only symptom of this affection, and of syphilis of the nervous system altogether, is a series of epileptic attacks, which in so far as the attacks alone are concerned may be indistinguishable from those of "idiopathic" epilepsy. The alterations in speech are sometimes of either an aphasic or an articulatory nature, but often are neither, consisting merely in a thickness of enunciation like that of great fatigue.

The syphilitic affections at the base of the brain are perhaps the best known and most frequent of all. From the fact that the lesions are most often extra-cerebral it is comprehensible that the symptoms are predominately those of affections of the cranial nerves. Of these some are much more often implicated in the disease process than others, and this

is especially true of the ocular nerves. Uhthoff, who has perhaps had the largest experience in the matter, states that they are in one way or another affected in 85 per cent. of the cases of cerebral lues. The optic nerve itself is frequently affected; this was the only ocular nerve to be so in 20 per cent. of Uhthoff's cases, and he found changes in it in fourteen out of seventeen autopsies on cases of cerebral syphilis. It may be affected primarily, *i. e.*, from an intra-neural gumma or degenerated arteries, or secondarily, from disease in the pia mater. The ophthalmoscopic signs differ according to whether the lesion present is a choked disc, an optic atrophy, or a descending optic neuritis; this is the order of frequency of the lesions. In the commonest condition, that of choked disc, the swelling of the disc and the distension of the veins are greater than in the cases of optic neuritis, but the opaque swelling of the retinal tissue with hæmorrhages and white spots around the macula are not so marked. On the side of the symptoms the following points are noteworthy: the defect in vision rarely goes on to complete blindness, as it so often does in cases of tumor cerebri and hydrocephalus; under treatment all symptoms and signs may in lucky cases altogether disappear; the perimetric changes are very variable, but on the whole the periphery of the field suffers most with a parenchymatous neuritis, and the central portion with a secondary perineuritis. The optic chiasma is a favourite site for syphilitic processes, which may then either descend or ascend. Hemianopsia is by no means an uncommon occurrence; it is stated that 10 per cent. of all cases of homonymous hemianopsia are of syphilitic origin, and 15 per cent. of all cases of heteronymous. The former kind is more frequently met with than the latter, and when the hemianopsia is heteronymous it is practically always bitemporal; there is only one instance on record of syphilitic binasal hemianopsia.

The motor nerves of the eye are also affected with extreme frequency. It is probable that more than half of all cases of ophthalmoplegia are due to syphilis. As a rule it is a relatively late affection, but cases are on record where the onset was as early as three months after infection. Any part of the nerve may be implicated, from the nucleus to the muscle; the commonest lesion is gummatous meningitis which has caused either compression or infiltration of the nerve substance. Of the three nerves in question the oculo-motor is the one most commonly affected, in two-thirds of the cases; Uhthoff's figures are: oculo-motor 66 times, abducens 29, of the cases; Uhthoff's figures are oculo-motor 66 times, abducens 29, trochlear 6. Bilateral symptoms are rather more frequent than unilateral; partial paralyses, of one or more muscles, more than total ophthalmoplegia. Of the external ophthalmoplegias ptosis is considerably commoner than any other; the internal ones concern predominantly the pupillary reactions. Non-reaction of the pupil to light may be throughout the only symptom of cerebral lues, or it may be the only one to remain after the others have disappeared under treatment. In general it must be said that luetic oph-

thalmoplegias are more refractory to treatment than other luetic conditions. The three chief diseases from which they have to be distinguished are tabes, cerebral tumour, and disseminate sclerosis. There is no absolute point of distinction as regards the eye symptoms between tabes and cerebral lues; one has always to depend on evidence obtained elsewhere. Still one may say in general that bilaterality, totality and durability are features that point to the latter condition rather than to the former, and that a dissociated pupillary paralysis (Argyll-Robertson sign), or a pronounced optic atrophy, points more to tabes. The paralyses of disseminate sclerosis are more often transitory and incomplete; nystagmus is usually present, but not pupillary fixation to light.

Basal syphilis produces of course other symptoms than those just mentioned; amongst them should especially be mentioned headache, vertigo, affection of other cranial nerves, particularly the trigeminal, facial and acoustic, and pareses of the limbs.

Some general remarks may now be made concerning the diagnosis of syphilis of the nervous system; it is impossible here to enter into the matter of differential diagnosis. In the first place I would warn against attaching too much importance to a positive or negative history of previous infection. The various fallacies in both directions are so numerous and gross that one is in this way easily lead into error. A negative history proves nothing at all, and should never even weigh against the diagnosis of syphilis if there is reason to make it. A positive history is chiefly of value in countries such as many parts of Ireland and Canada, where syphilis is as yet relatively rare; in most parts of the world the information that a patient has probably had syphilis is not novel enough to be of much significance in deciding whether a given group of symptoms are or are not due to this disease. A positive Wassermann reaction, on the other hand, is another matter, since, in the absence of certain tropical maladies, it demonstrates the present activity of a syphilitic process. Care however should be taken that the reaction is carried out by a specially competent person, and with the original technique; some of the modifications recently attempted, notably those by Noguchi in this country, are quite unreliable. Again, the fact that the date of infection is unusually recent or remote should not weigh too much against the diagnosis of cerebro-spinal syphilis; cases have been reported as recently as two months after the infection and as long as forty years after, though most often they occur between the first and sixth years.

The distribution of the lesions and the course run by the disease is an important matter. Irregularity is here the rule: numerous areas of the nervous system are picked out in apparently the most haphazard way, and the symptoms may fluctuate from time to time to such an extent as almost to suggest a psychogenic malady. It should be borne in mind that most syphilitic lesions are on or near the surface of the nervous system; one would hesitate very much before making the diagnosis of

syphilis when the symptoms pointed to a deep-seated lesion, *e. g.*, a thalamic tumour. Here the general rule of neurological diagnosis is of especial value—namely, that one should first try to determine the *site* of the lesion, then the pathological nature of it, and only lastly its cause.

Finally a word should be said about the diagnosis by means of anti-syphilitic drugs. This is a method open to serious error, for on the one hand cerebro-spinal syphilis is often notoriously refractory to such measures, whereas on the other hand they frequently have a temporary influence on non-syphilitic affections of the nervous system. The point is of especial practical importance in regard to the diagnosis of cerebral tumour, a matter that has not here been discussed. Fibrous gummata are, perhaps, more resistant to drug treatment than any other syphilitic lesion, and in many cases it is advisable to remove them by operation. On the other hand, with non-syphilitic tumours, *e. g.*, gliomata, valuable time is often lost through the encouragement given by a temporary relief of symptoms that has been brought about by drugs. In a case of cerebral tumour the practice should always be to operate at once provided the Wassermann reaction is negative, and never to wait to see the effect of drug treatment.

The prognosis of cerebro-spinal syphilis is in general a serious one, owing to the frequency with which it resists treatment, and to the pronounced tendency to late recurrences and grave complications. Various factors affect the outlook. For instance, this is worse in cases where the onset of the disease is many years after the date of infection, or when other diseases or cachexias are present, particularly tuberculosis and alcoholism; it seems to be worse also in cases where the early manifestations of syphilis were slight. Unfortunately there is not much reason to believe that thorough treatment in the early stages is a satisfactory guarantee against the later occurrence of cerebro-spinal syphilis, but on the other hand energetic treatment at the onset of this certainly has an important influence on the course it will run.

We have last to consider a few points concerning parasyphilitic affections of the nervous system. These affections are of especial importance in that they are commoner than true cerebro-spinal syphilis, are even more serious in their effects, and resist anti-syphilitic treatment. It is not definitely proved that there is any other parasyphilitic affection than general paralysis and tabes, though it is very possible that certain forms of progressive spinal muscular atrophy are also of this nature. As general paralysis and tabes are essentially the same disease, differing merely in their distribution and course, they may here be considered together. The inference reached years ago on deductive grounds, that these conditions cannot occur without a previous syphilitic infection, may to-day be regarded as conclusively proved, so that the evidence need not here be recapitulated.* In the case of general paralysis, the form that has been most

*See Ernest Jones: The Pathology of General Paralysis. *Alienist and Neurologist*, November, 1909, p. 577.

extensively investigated, the blood serum gives the specific Wassermann reaction with such constancy that the absence of this is sufficient to exclude the disease; even with the cerebro-spinal fluid the reaction is positive in 95 per cent. of the cases. With tabes the reaction is for certain definite reasons less constant. Research along these bio-chemical lines has taught us much concerning the pathogeny of the disease.* It is highly probable that tabo-paralysis is not a direct consequence of the nervous system being poisoned by the syphilitic virus, but that it arises, so to speak in the way of a by-product, as a result of the metabolic changes that are concerned in the production of specific responses to this virus. It is even possible that the so-called Wassermann anti-body is the actual pathogenic factor, though probably the matter is more complicated than this.

It is not necessary here even to outline the well-known clinical manifestations of tabo-paralysis, but a word may be added on some recently acquired aids to the diagnosis of it, thanks to which we are nowadays practically always able to make it with certainty. The value of the Wassermann test has just been referred to; it is especially useful in differentiating the condition from cerebro-spinal lues, for in this the reaction is at least five times less common with the cerebro-spinal fluid than it is in tabo-paralysis. Unfortunately it often happens that application of the test is inconvenient or impossible, owing to the inaccessibility of a special laboratory. In these cases the other evidence that may be gathered from clinical examination of the cerebro-spinal fluid is of great value, for this can be obtained by any practitioner. The two most important aids here are the cell-count and the proteid estimation. In no other chronic condition is such a high cell-count seen as in tabo-paralysis, and when it exceeds forty or fifty one can be almost certain that we have to do with this disease; the diagnosis can be confirmed by a differential examination carried out by Alzheimer's method. A still simpler matter is the investigation of the globulin content, which is considerably increased in this disease.** Many tests have been devised for this purpose, by Nonne and Apelt, Pandy and others. In my experience the two most reliable are the Noguchi butyric acid test, and the ammonium sulphate ring test described by Ross and myself. Of the two I have found the former more valuable in a negative direction and the latter in a positive.

The subject of treatment has not been touched on in this paper, as it will be dealt with by other contributors to the present symposium. As to the marvellous Ehrlich-Hata discovery it seems at present that so far as cerebro-spinal syphilis is concerned this will be of more value for prophy-

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*See Plaut: Die Wassermannsche Serodiagnostik der Syphilis in ihrer Anwendung auf die Psychiatrie. 1909; and Ernest Jones: A Review of Our Present Knowledge Concerning the Sero-Diagnosis of General Paralysis. *Amer. Jour. of Insanity*, April, 1909, p. 653; Modern Progress in Our Knowledge of the Pathology of General Paralysis. *Lancet*, July 24, 1909, p. 209.

**Ernest Jones: The Proteid Content of the Cerebro-Spinal Fluid in General Paralysis. *Rev. of Neurol and Psychiatry*, June, 1909, p. 379.

laxis than for treatment. If the present high promise of this remedy is fulfilled it will be by no means Utopian to anticipate a day when syphilitic affection of the nervous system will become a rare disease. Such a triumph of medical science would be a check to certain lines of neuro-pathological research, but in my opinion this would be more than compensated for by the much-needed impetus it would give to non-histological, *e. g.*, psychological, lines of psychiatric investigation.

THE TREATMENT OF SYPHILIS WITH EHRLICH-HATA "606"—SALVARSAN.

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It must be apparent to all by this time, that the genius of Paul Ehrlich has given to the therapeutics of syphilis the most potent remedy that has ever been known. Many thousands of cases have already been treated with this new remedy, in the hands of numerous clinicians, and with exceedingly few exceptions, all are agreed that this new preparation constitutes a most invaluable addition to our armamentarium in the management and control of syphilis.

This preparation is intended to reach the parasites in the body which cause the disease, *i. e.*, the spirochetes pallida, and destroy them in one dose, in accord with Ehrlich's chemo-therapy. For many years, he aimed to find a substance that was not only destructive to the parasites (parasitotropic), but at the same time, not injurious to the body of the host (organotropic). Ehrlich believes that the new arsenobenzol preparation, or as it has been named, *Salvarsan,* is not organotropic but parasitotropic, and hence the ideal remedy for a cure of the disease by the method of "therapia sterilisans magna." Indeed, clinical evidence is accumulating every day, in all quarters of the globe, that this belief of Ehrlich has been substantiated by actual test.

Already a large literature has grown up, particularly in German, giving detailed accounts of the chemical and physiological action of the drug, and illustrating by description of actual cases the method of its action. Hence, it is not deemed necessary, in this paper, to discuss these features of the remedy; the list of articles and papers thus far published on the subject may be found in the excellent collection of references published by Fordyce,* Engelbach,** and Stein.† The principal contributors and pioneers in the use of the new remedy have been Iversen, of St. Petersburg; Alt, of Uchtspringe (near Berlin), and Wechselmann, of Berlin. These were the first to use the drug, and their particular methods of administering it are used generally wherever the drug is being experimented with. The intravenous method, *i. e.*, the injection of a very dilute alkaline solution into the veins, is known as Iversen's Method; the intramuscular injection of an alkaline solution, is known as Alt's Method;

*Fordyce: *New York Medical Journal*, November 12, 1910.
**Engelbach: *Interstate Medical Journal*, October, 1910.
†Stein: *Medical Record*, November 5, 1910.

and the injection into the muscles or subcutaneously of a neutral emulsion, is known as Wechselmann's Method.

Last summer, through the kindness of Professor Ehrlich, I was given a supply of the drug for clinical use, and though it is but six weeks since I gave my first injection, which would preclude the possibility of drawing conclusions as to the permanency of the results obtained, there has been sufficient evidence to indicate the wonderful possibilities that obtain with this new preparation. A sufficient number of cases have been observed, not only in my own experience at home, but also while abroad, in the clinics of Wechselmann, Michaelis, Kromayer and others, to make it possible to point out the practical methods of application of the drug, and the phenomena that might be expected to follow its administration.

I believe the drug should not be used in every case of syphilis, particularly just now when its use is still more or less in the experimental stage, and while we are learning the first steps in its use. I have used the drug only in those cases, (1) that would determine its efficiency in certain distinct lesions; (2) where manifest conditions or lesions were present that might be traceable to syphilis; (3) where mercury and iodides have been of no avail; (4) where neither mercury nor iodides have been used. In other words, only such cases that give unmistakable, palpable lesions, were accepted for treatment. This policy gave the drug a distinct problem to meet and overcome in each case. I do not consider the mere presence of a positive Wassermann without lesions, a sufficient reason for administering the treatment.

In considering the treatment of syphilis with the new remedy three questions suggest themselves: 1. Is the new remedy a specific for syphilis, and is it superior to previously known remedies? 2. Does it cure syphilis permanently? 3. Are the dangers of the remedy proportionate to the importance of its action? These questions were first asked in June, 1910, by Wechselmann, to whom Ehrlich entrusted the remedy for trial in his service at the great Rudolf Virchow Hospital, Berlin. I feel safe in saying that our experience of the past six months, with this remedy, making due allowance for the exuberance of enthusiasm for a new therapeutic aid, justifies us in answering these questions with a reasonable degree of optimism.

As to the first question: *Is it a specific in syphilis?*—The answer is to be found in the innumerable cases in which syphilitic lesions have responded to the influence of this remedy in a manner never hitherto seen. Cases that have resisted mercury to the point of salivation and iodides to the point of tolerance, have responded most favorably to this arsenic preparation. I believe that it is a specific in syphilis, though it would be presumptuous to say that it will cure every case of syphilis, any more than we can say that quinine will cure every case of malaria. I have not yet seen a syphilitic lesion that did not show a greater or less response to the drug, and on the other hand, it has often proven the existence of

syphilis in cases where mercury and iodides failed to do so. We thus find the remedy not alone therapeutically efficient, but also uncovering hidden and undiagnosed conditions dependent upon the presence of syphilitic disease. It is thus apparent that this drug will soon assume an important place as an aid and complement of the Wassermann serum reaction, in the diagnosis of obscure syphilitic conditions. Is it superior to mercury? The cases are too numerous to mention in which it has caused the disappearance of lesions that had resisted mercury and the iodides for years.

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Fig. 1. W. S., October 17, 1910. Just before injection of 0.5 gm.

In fact, its most astonishing results are seen in just those cases, particularly tertiary lesions, that have not been influenced by these drugs.

(2) *Does it cure syphilis permanently?*—The future alone can answer this question. Undoubtedly some cases will relapse, but this may be due to insufficient dosage, faulty technique, or some other at present unknown cause, that time itself will reveal. All that can be said thus far, as to permanency, is that by far the greatest proportion of cases that have been treated have stayed well, some of them, almost if not quite a whole year or more, after a single injection. We must wait and see how these cases develop, before we say anything definite as to permanency, but mean-

while there is sufficient evidence at hand that Ehrlich's sole aim,—a therapia sterilisans magna, has been accomplished in a large number of cases, as far as present indications show.

(3) *Are the dangers of the remedy proportionate to the importance of its action?*—Here, too, time and further experience must answer. Some 40,000 injections of the remedy have already been made, and as far as I can gather, there have been not more than twelve to fifteen deaths following the treatment. Among this number are some which cannot rightly be ascribed to the drug, but even conceding that they may, the

Fig. 4. W. S. Taken October 29, 1910. Twelve days after injection of 0.5 gm.

percentage of serious risk would seem to be very small,—one death to three or four thousand. It stands to reason, there must be some risk attached to the introduction of a remedy that aims at one blow to rid the organism of all its attacking parasites. Ehrlich himself has often stated that any drug that can completely destroy all the parasites in the body at one blow cannot be without some danger. Possibly the endotoxins liberated by the sudden death of these innumerable parasitic bodies, may constitute a risk; possibly also, a maximum of absorption with a minimum of elimination of the drug may have caused these deaths. We must not

forget that a full dose of the remedy contains about three grains of organic arsenic. This amount of arsenic must be taken up by the organism and eliminated after the work is done. Fischer and Hoppe, pioneers in this work, showed that in a patient who received an injection of 0.3 grams (containing 0.12 gm. of organic arsenic), organic arsenic was found in the urine 12 days after the injection, and the amount recovered was 0.0506 gm. In other words, about one-half of the total amount injected. A similar proportion was found in other cases. These data would indicate that about one-half of the amount injected must be eliminated by the kidneys. A smaller percentage is also excreted through the skin and feces. It is thus apparent that if the excretory functions are not adequate to the task of ridding the organism of this excess of arsenic, a storage of the drug may take place in the tissues, and toxic results may

Fig. 2. W. S., October 17, 1910. Just before injection of 0.5 gm.

Fig. 5. W. S., October 29, 1910. Twelve days after injection of 0.5 gm.

follow. Likewise, it seems possible, that an improper technique may introduce septic material or other foreign products, which may act in a manner detrimental to the body-tissues. In short, the greatest risk in the administration of the remedy is to be found in an insufficient excretory function. I am convinced there is no very great risk inherent in the drug itself; in other words, it is not organotropic while it is distinctly parasitotropic, as far as the spirochetes pallida are concerned.

Indications for its Use in Practice.—These are summed up by Blaschko as follows:—

(a) Malignant cases of syphilis which have not reacted to mercury.

(b) All forms and stages of syphilis in individuals who show an idiosyncracy towards mercury.

(c) Cases in which recurrence occurs soon after mercurial treatment.

(d) Cases in which recurrence occurs while the patient is taking mercury.

(e) Primary lesions before the appearance of secondaries.

(f) Constitutional syphilis not hitherto treated in the primary or secondary stages.

(g) In late recurring secondary lesions it should be used in combination with mercury and iodides.

(h) In parasyphilitic affections of the cardio-vascular and nervous systems, it should be used only in the early stages.

Ehrlich recommends that primary lesions should be treated as early as possible, before the appearance of secondaries, adding that energetic

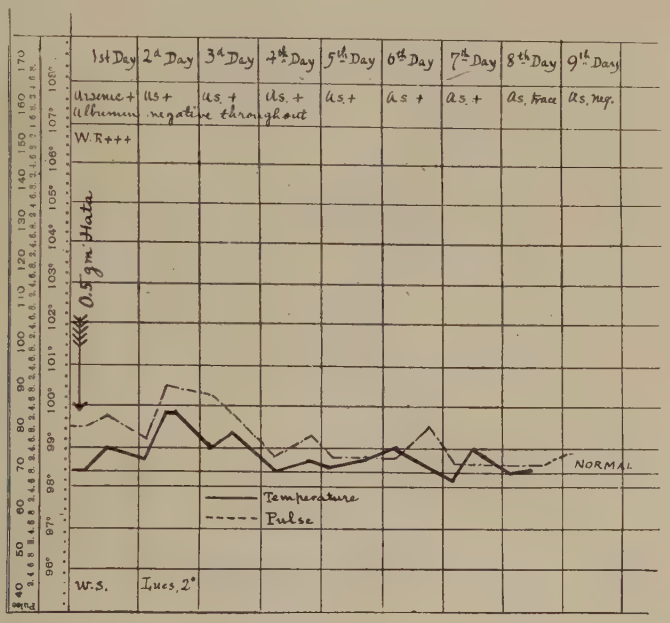


Fig. 3.

local treatment should be employed, to aid in causing complete sterilization, such as excision, cauterization and other methods of destruction.

Contraindications against its use:—

(a) Advanced disease of the nervous system, and general debility.

(b) Distinct lesions of the cardio-vascular and renal functions.

(c) The existence of an idiosyncracy towards arsenic.

(d) Pregnant women seem to tolerate the drug well, but in some instances abortion seems to have been caused by it.

It should be noted in this connection, that the presence of albumin and casts in the urine, in small quantity, is not a contraindication, *per se*. Cases have been reported in which a persistent albuminuria with casts has been cleared up after the injection, and on the other hand a specific

albuminuria with or without casts will nearly always disappear under this treatment.

Technique.—From personal observation and experience, I believe that the method of Alt (alkaline solution) mentioned above, is the simplest to carry out, and is perhaps the most effective. I have used it in all my cases, numbering about thirty-five, with satisfactory results. It is as follows*:—

With a glass pipette, 10 c.c. of hot distilled water are put into a glass mortar, having a capacity of 50 c.c.; to this is added the arsenolbenzol a little at a time, constantly stirring it with a pestle, until it is thoroughly dissolved. We now have a clear, amber colored solution, strongly acid. With another pipette, we add a four per cent. solution of sodium hydrate in sterile distilled water, about 0.5 c.c. of the solution for each decigramme of powder used, constantly stirring with the pestle. Now a thick gelatinous mass forms, in which the substance is precipitated; but by continuing to add the sodium hydrate solution, drop by drop, the precipitate disappears and another solution, quite clear, is now formed. This solution is very strongly alkaline, and if thus injected causes much pain. In order to diminish the alkalinity, and make the solution nearly neutral (and consequently painless), we add, drop by drop, through a third pipette, a one per cent. solution of acetic acid (in sterile water), constantly testing with litmus paper. When the alkalinity is reduced to a minimum, sufficient distilled water is added to make 20 c.c., and of this solution, 10 c.c. is injected into each buttock. A piece of sterile gauze is now placed over the site of the injection and held in place with two strips of adhesive plaster, forming an X. The patient should lie face downward for about half an hour, and should then be put to bed and kept there for a day or two. He should now be kept under careful observation, for at least one week, preferably a fortnight, in the hospital or at home.

Certain precautions are absolutely necessary and should never be omitted. All the apparatus used for the injection should be thoroughly sterilized in the same manner as surgical instruments before operation. This includes the mortar and pestle, the syringe and needle, the pipettes, and even the steel file with which the neck of the glass vial containing the powder is cut across. The neck of the vial should be cleansed with alcohol and ether. The skin of the buttocks should be thoroughly cleansed and rubbed with ether until it is red, immediately before the injection. This helps to anesthetize the skin and renders the injection less painful.

Another very important precaution to be observed is that the solution should be made up immediately before it is to be used, at the bedside of the patient. The best results are obtained only when the solution is absolutely fresh and sterile.

The operator should wash his hands carefully, and wear a sterile gown. The needle employed should be fairly large in calibre, similar to the one used in the injection of the insoluble mercury preparations. A Record syringe with a capacity of 20 c.c. is the ideal instrument for this purpose. Care should also be taken not to inject the fluid into a vein or an artery.

Preliminary Examination Previous to Treatment.—In every case I have had a thorough examination made of the lungs, heart, arteries, and abdominal organs. The eyes have been carefully examined, especially the fundus; I have been informed by Alt and Wechselmann (personal com-

*Wolbarst: *New York Medical Journal*, November 12, 1910.

munications), who have used the drug in thousands of cases, that they have never seen any ocular complications, even in cases of optic atrophy. A Wassermann test is made in every case, and if a skin lesion is present,

Fig. 6.

an examination for spirochetes is made. Especial attention is paid to the urine, as the presence of sugar, albumin and casts in large quantity, is a contra-indication to the use of the drug.

Phenomena Following the Injection.—Certain phenomena stand out prominently in all cases after the injection, and it is well that they should be anticipated.

1. There is usually a distinct rise of temperature. The average rise is up to 101° F., but 102° is not unusual, and one of the cases mentioned below showed a temperature of 105.4° F.

2. The pulse does not vary much from the normal.

3. Whatever pain the patients may have, they usually eat well, feel good and do not at any time "look sick." The temperature is not that of a febrile disease.

4. In the gluteal injection, the buttocks will often feel "sore" for a number of days after the injection. Sitting on a chair is a painful operation. I have observed, however, that necessity devises a way of obviating this inconvenience. The patients sit astride the chair, facing the back, with a pillow or cushion on the seat. This seems to make the process a painless one.

5. It is interesting to note the gain in weight in most of these patients. The rate of gain is about a pound a day, in the average case.

6. Patients with tabes dorsalis seem to be insensitive to the injection itself. However, their accustomed pains in the legs often appear some time after the injection.

Perhaps the best way to illustrate these phenomena, is to report in full several cases, each of them representing a distinct set of phenomena and symptoms. Particular attention was paid in every case to the temperature and pulse, the excretion of arsenic and albumin in the urine, the weight of the patient, and the condition of the eyes. In a few instances, some particular detail was omitted through the inability of the house staff to carry it out, at the time. The period of observation in the hospital, ranged from ten days to two weeks; thereafter the patients were seen twice weekly, to date, wherever possible.

Case I. *Secondary Syphilis Rebellious to Mercury and Iodides.*—W. S., male, aged twenty-three, referred by Dr. E. M. Hawks. Previous history negative. Initial lesion on penis in May, 1910. Roseola appeared on body last week in June. Macules slowly changed to pustules, and were not influenced by treatment. Condition, October 1st, 1910, pustules on back, ranging in size from a dime to a quarter; have slowly dried, and become scaly (Fig. 1). Mucous patches on tongue since July; have remained and become ulcerous. Slough over both tonsils during August and September. Left iritis since September 15th. Ulceration on great toe (Fig. 2) since early in September. Nail removed October 14th. He has lost much flesh and strength.

Treatment: Hydrarg. succinamid. gr. 1/5, three times weekly, by hypo; 15 injections; no result. Salivated first two weeks in August. Last two weeks in August, protoiodid of hydrarg, gr. 1/3 per mouth; salivated again. Inunctions since September 7th. 15 (30 grains), 8 (40 grains); also KI. No effect. October 16th, Wassermann Reaction + + + +.

October 17th, received 0.5 gm. Arsenobenzol; Alt method. Pain moderate, radiating principally down the thighs, and controlled by hot water bag on but-

tocks. Reaction not marked (see temperature chart, Fig. 3). Uneventful stay in hospital; up and about on the second day. Temperature highest on second day (99.8° F.). No infiltration nor redness at site of injection. Tender on pressure.

Examination of eyes, by Dr. M. Rosenbaum: "October 24th, syphilitic iritis of left eye; slight circumcorneal injection, posterior synechiæ, cloudiness of vitreous.

October 28th: Cloudiness of vitreous disappeared, iritis not present; posterior synechiæ fading. Right eye normal; left eye, vision 12/70 with atropin.

November 3d: Both eyes normal."

Discharged from hospital October 29th. Skin lesions but faintly visible; pink spots on back. Scaling all disappeared. Great toe granulating. (Figs. 4 and 5).

November 18th: Eyes normal; skin still shows pink areas where the ulcers formerly were. Patient has gained nearly fourteen pounds. Big toe nearly well, with new nail rapidly coming out.

December 13th: Skin clear; toe practically well; eyes normal. Wassermann reaction + +.

A study of the temperature chart (Fig. 3) will point out several features of this case. The temperature curve, indicates that the reaction was not a severe one; usually the temperature reaches 101° or 102° on the second day, but in this case it did not rise above 99.8° F. The pulse acted in harmony, and did not pass 90 per minute. Arsenic was found in the urine within eight hours after the injection, and could be determined daily eight days thereafter. On the ninth day none could be observed. Albumin was absent throughout. The Wassermann reaction, 57 days after the injection, is still positive.

Case II. *Malignant Secondary Syphilis, Resisting Mercury and Iodides.*—J. L., male, aged twenty-eight, referred by Dr. J. B. Prager. Initial infection eighteen months ago, on the penis. Began as a pustule, which grew large and hard and eventually broke down, resisting treatment for seven months. Inguinal glands swollen and tender. Six weeks later, the roseola appeared and disappeared only after several months of treatment. For the past three months the patient complains of a sore throat, growing worse all the time, so that it interferes with his speech and renders swallowing difficult and painful. Has also had pains in the joints.

Examination of the eyes, heart, lungs and kidneys negative. Wassermann reaction + + + +.

Examination of the throat revealed a large greenish white, ulcerating area covering the uvula, tonsils, post-pharyngeal space, and part of roof of the mouth (Fig. 6). The mouth could be opened only with difficulty.

November 3rd, 1910. Injected 0.5 gm., Hyperideal. Alt method. No pain at time of injection, but a few hours later, pain of moderate severity over the site of injection which lasted two days. Throat was cleansed with saline solution.

November 5th, improvement noted. Green ulceration turning paler and assuming a brownish color. Throat feels better, swallowing and speech easier.

November 10th, improvement continuous. Full diet. Out of bed and feels better in every way. Ulcerated area assuming normal color. No infiltration nor redness at site of injection.

November 15th, left the hospital feeling perfectly well, though the throat still showed some signs of the recent ulceration.

November 20th, throat normal.

November 25th, throat normal, and patient back to work. Gained seven pounds. Has not returned for further observation.

In this case the typical temperature reaction is observed (Fig. 7). The temperature reached 102° on the second day, the pulse going up to 112. Then a decline followed. During the reaction, the patient did not look sick. This is a peculiarity of this metabolic reaction to the drug. Arsenic was found in the urine for five days after the injection. Albumin was negative except on the second and third days after the injection. The quantity of urine passed was normal throughout. The eyes showed no changes at any time.

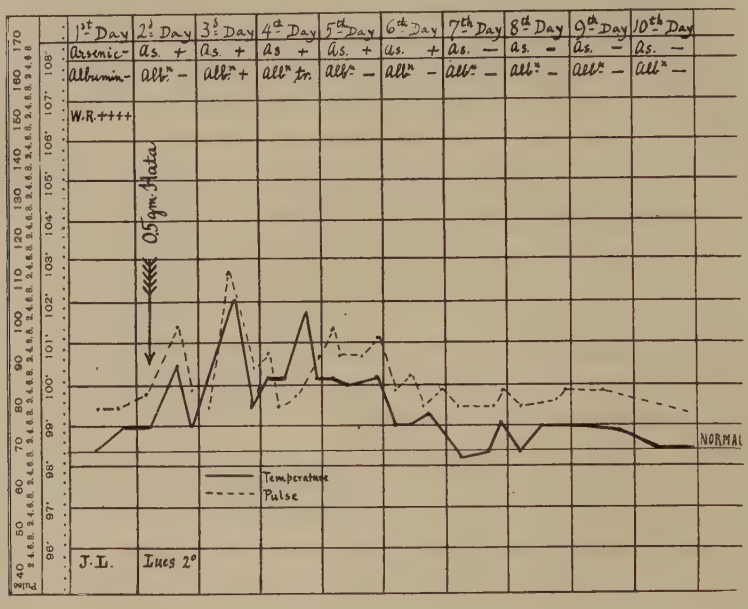


Fig. 7.

Case III. *Primary Affection.*—R. E., male, aged twenty-seven, referred by Dr. S. W. Bandler. Good general health. Initial lesion on shaft of penis, near corona, hard and typical in appearance, the size of a quarter. Duration two weeks. No secondaries. Inguinal glands indurated, not tender. Other glands negative.

November 4th: Examination for spirochetes, *positive.* Wassermann reaction, *negative.* Acting on the suggestion of Ehrlich, that these initial cases be treated as early as possible, preferably with excision of the lesion, an injection of 0.5 gm. Hyperideal was given November 7th, 1910. Excision was suggested, but not permitted. To avoid any possible doubt as to the character of the lesion (in the absence of secondaries) patient was also examined by Dr. Ludwig Weiss, who confirmed the diagnosis. Examination of eyes, visceral organs and urine, negative.

November 7th, 0.5 gm. Hyperideal. At method. Pain moderate, but in a few hours it extended down the thighs, and remained there for several days. Controlled somewhat by hot applications, and gr. ¼ morph. at bedtime. In the

afternoon the temperature rose suddenly to 102° F. Pulse 76. A study of the temperature curve (Fig. VIII.), shows an unusually active response to the drug.

1st day, 99.5° to 102.0°; pulse 64 to 76.
2d day, 97.0° to 101.8°; pulse 68 to 80.
3d day, 100.1° to 102.6°; pulse 68 to 100.
4th day, 100.6° to 102.0°; pulse 98 to 100.
5th day, 102.0° to 101.0°; pulse 96 to 92.
6th day, 101.2° to 103.0°; pulse 92 to 96.
7th day, 103.0° to 104.5°; pulse 90 to 102.
8th day, 104.5° to 105.4°; pulse 90 to 102.
9th day, 105.4° to 103.8°; pulse 100 to 95.
10th day, 103.8° to 103.2°; pulse 95 to 90.
11th day, 103.2° to 100.8°; pulse 90 to 85.
12th day, 100.8° to 99.0°; pulse 85 to 72.
13th day, 99.0° to 98.2°; pulse 72 to 70.
14th day, Normal. Normal.

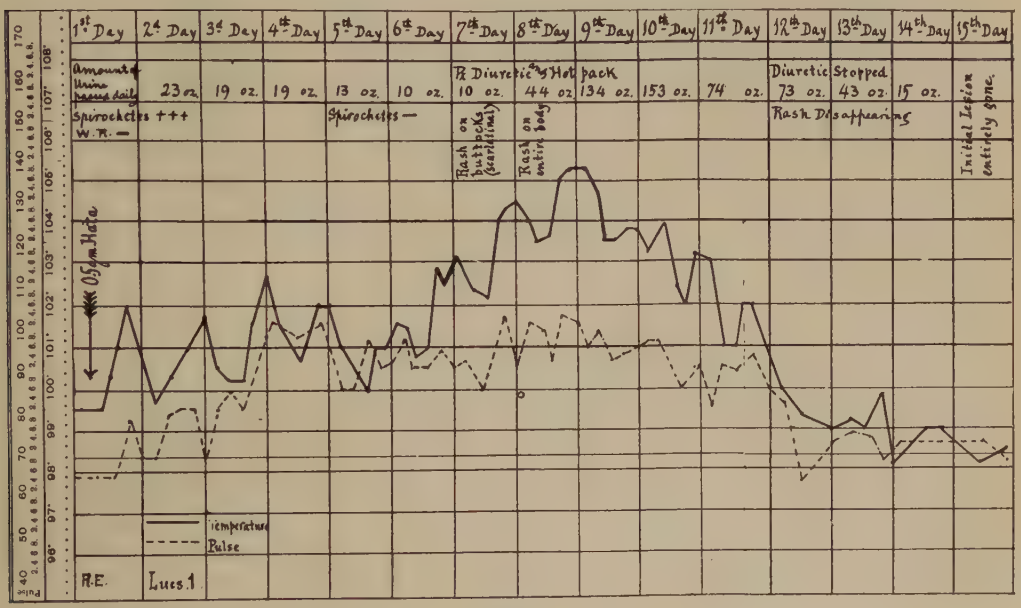


Fig. 8.

Interesting features of this case that are unusual, are the very high temperature, partial suppression of urine, and coincident appearance of a generalized scarlatinal rash. The amount of urine passed on each day after the injection is as follows:

1st day, amount not counted.
2d day, 23 ounces.
3d day, 19 ounces.
4th day, 19 ounces.
5th day, 13 ounces.
6th day, 10 ounces.
7th day, 10 ounces. Rash on buttocks (diuretic given).

8th day, 44 ounces. Rash on entire body, scarlatinal.
9th day, 134 ounces.
10th day, 153 ounces.
11th day, 74 ounces. Rash disappearing.
12th day, 73 ounces. Diuretic stopped.
13th day, 43 ounces.
14th day, 15 ounces.

The rash appeared coincidently with the high temperature and urinary suppression; it first appeared on the buttocks (site of injection) and soon spread to the rest of the body, including the face; the urinary condition was relieved by a strong diuretic and hot packs, with plenty of water internally. During all this time the patient did not feel unwell in the least, except for the pains in the legs, and in the arms. These were somewhat relieved by alcoholic rubs. There seemed to be a neuritis, possibly of arsenic character. The patient was rather dull and slept a good deal. Otherwise felt well. The tongue was coated with a yellowish white, thick, slimy fur, which I have only seen in similar cases with high temperatures. Unfortunately at the time there were no arrangements for the examination of the urine for arsenic. However, there can be no doubt that the entire complex of symptoms was due to faulty elimination of the drug, or hypersensitiveness (idiosyncracy) to the drug, or both.

November 11th. Spirochetes negative. Chancre soft and fast disappearing; glands negative. No infiltration or redness at the site of injection.

November 15th, discharged from hospital. Primary lesion gone, except a slight pinkish discoloration of the skin and slight thickening.

November 30th, Wassermann reaction + + +. Skin clear, glands negative, patient has gained about ten pounds. Eyes normal.

December 4th, Wasserman reaction + +; skin clear, patient normal and feels well.

Case IV. *Tabes Dorsalis, Optic Atrophy (partial). Gastric Crises. Marked Ataxia.*—J. M., male, aged thirty-six. Denies venereal history of any kind. First symptom of illness appeared six years ago, in the form of gastric pains, accompanied by occasional attacks of vomiting. Was treated for gastric disease until six months ago, when the diagnosis of tabes dorsalis was made by Dr. George J. Saylin, of Buffalo, N. Y. These symptoms were then present: Absence of knee-jerk, marked ataxic gait, Romberg symptom, Argyll Robertson pupil, gastric crises with vomiting, shooting and lightning pains in legs. Optic atrophy, loss of flesh and strength. Wassermann reaction strongly positive. Urine negative as to sugar and albumin. Was put under treatment consisting of injections of salicylate of mercury and arsenic. Strychnin internally for the optic atrophy.

October 21, 1910. Marked ataxia, necessitating use of two canes and other support. Stumbles in the dark. All diagnostic symptoms of tabes marked and unmistakable. Eyes examined by Dr. E. Gruening: "O. D. 3/100; O. S. 3/200. Both normal fields concentrically limited. Absolute color blindness. Optic atrophy."

Examination of viscera, heart, lungs and kidneys, normal. Pulse 96, not very strong. Wassermann reaction + + + +.

At the earnest solicitation of the patient, and his assuming all liability as to the outcome, he was admitted to the hospital.

October 24, 1910. Injected 0.5 gm. arsenobenzol. Alt method. No pain whatever at the site of injection, during his entire stay in hospital. Six hours after injection, pain appeared in the legs and around the chest. These did not differ in any way from his accustomed pains. Vomiting also set in on the second day, and continued for three days, after which period it ceased. Like-

wise the pains. The pain and vomiting did not differ in any way from his accustomed crises.

October 28th, out of bed, in ward. Walks without a cane. Thinks his gait is less ataxic. With his eyes closed sways much less than previously. Pain absent. Eyesight not as good as before. Examination by Dr. Rosenbaum: "Atrophy somewhat advanced. Vision diminished. O. D. Fingers at five feet; O. S. Fingers at three feet. Previous to injection, O. D. Fingers at seven feet; O. S. Fingers at five feet." No infiltration or redness at the site of injection.

The temperature chart shows an unusual curve (Fig. 9). It will be seen that the patient reacted slightly on the day of the injection, by a lowering of the temperature to 98°, and on the third day there was a still further decline to 97° F. This decline was soon changed to a slight elevation, never exceeding

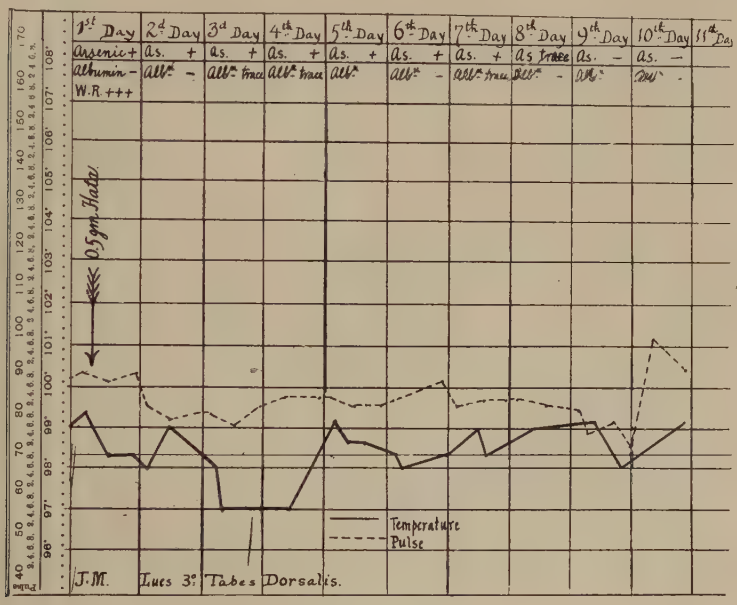


Fig. 9.

99.5°. It will be seen that the pulse did not share in the great lowering of the temperature. Arsenic was found in the urine eight days after the injection.

November 2, 1910, he left the hospital, under protest, feeling very well, except for his sight. He walked easily without a cane, though he showed a distinct ataxic gait. Gain in weight, four pounds.

November 16, came to office for observation. Walked without a cane. Felt much better.

December 3rd. Communication from his physician, Dr. Saylin, states: "Despite progressiveness of optic atrophy, gait and general condition show improvement. Patient is inherently hystero-neurasthenic,—yet, after careful observation, I can say that his condition has improved markedly, except his vision."

December 13th. Communication from Dr. Saylin, as follows: Wassermann reaction, December 10th, taken by Dr. A. A. Thibaudeau, is positive, but less strongly so than formerly.

As regards the physical aspects of the case, I can but reiterate that there is a positive improvement. His gait is rather that of a blind man than that of a

tabetic. Romberg's symptom, which was marked three months ago, is but slightly so now. He has gained in weight and complains less of weakness in his lower extremities and of the "carpet" sensation. Vesical atony which was characteristic in his case, also shows improvement. However, he states positively that his sight became worse and became markedly so shortly after the administration of "606." Tests prove him right, and this raises a question as to future procedure.

It will thus be seen that this patient has improved, as far as his gait and general condition are concerned, but the progress of his optic atrophy has apparently not been stopped. This is quite contrary to the general behavior of similar cases after the injection. In many thousands of cases examined by Fehr for Wechselmann (Berlin), there was no deterioration of sight after injection, even in cases of optic atrophy. The question to be determined in this case, is whether the deterioration in vision was hastened by the injection, or whether it would have occurred even without the injection. At any rate, the treatment, apparently was unable to stop its progress, though it benefited the patient in other respects.

Case V. *Lues* 3°. *Cerebral Syphilis.*—A. A., aged twenty-nine, referred by Dr. C. A. Spivacke. Father died of tuberculosis, mother still living, affected with diabetes. Patient has had several attacks of urethritis.

Primary affection in 1905. Was treated for about six months with mercurial injections. No history of sore throat, alopecia, or pains in head. A year later the right elbow became painful and swelled a great deal. The pain was dull in character and so severe at night as to keep him awake. This condition improved under treatment.

Eighteen months ago patient suffered an attack of right hemiplegia while under the influence of alcohol. The right arm, leg and right side of face were affected. In bed several weeks. Also suffered slight illusions at the time. He improved under a course of iodides, but felt very depressed and lost all ambition for work or play. The right elbow remained swollen and tender. Has been under treatment for some time at the Vanderbilt clinic.

I saw him first October 26, 1910. He was dull and apathetic, unable to do his work (bartender), losing one position after another. His face had a constant smiling, childish appearance. Had no illusions, but realized that he was not well and wanted to do anything that might enable him to go back to work to support his mother.

Physical examination as to viscera, heart and arteries, and urine, normal. The right elbow joint measured 11 inches in circumference, the left 10¼ inches. Eyes normal, except for a slight cloudy deposit on the anterior surface of lens of left eye, in upper right quadrant. Wassermann reaction + +.

November 3, 1910. Injected 0.5 gm. Arsenobenzol, Alt method. Slight pain, which passed off next day. Temperature reaction quite active (see Fig. 10). Never higher than 102° on the third day. Pulse varied from 70 to 94. Stay in hospital uneventful. Was out of bed most of the time. Improved markedly after the fourth day. His mind brightened up perceptibly, he took a greater interest in things about him, and expressed a strong desire to go home and back to work. He felt strong and able to do anything. No infiltration or tenderness at the site of injection.

November 8th, at my request he wrote me a letter describing his condition. It is full of hope and optimism; in fact, it gives every evidence of being written by a man who has awakened out of a stupor and sees the light of day.

November 15th. Sent home. Much improved. His arm does not pain any more and there is but a slight difference in the measurement of the elbows. His mind is active and bright, and his mother feels that he is brighter than he has ever been.

Arsenic was found in the urine eight days after the injection, albumin negative throughout.

December 1st. Condition highly satisfactory in all respects. Wassermann reaction + + +. Eyes normal.

It is hoped that these five cases will suggest the possibilities of the new remedy in syphilis and its allied conditions. Time and space forbid a complete report at this time of some of the other cases in this series, most of which are of unusual interest.

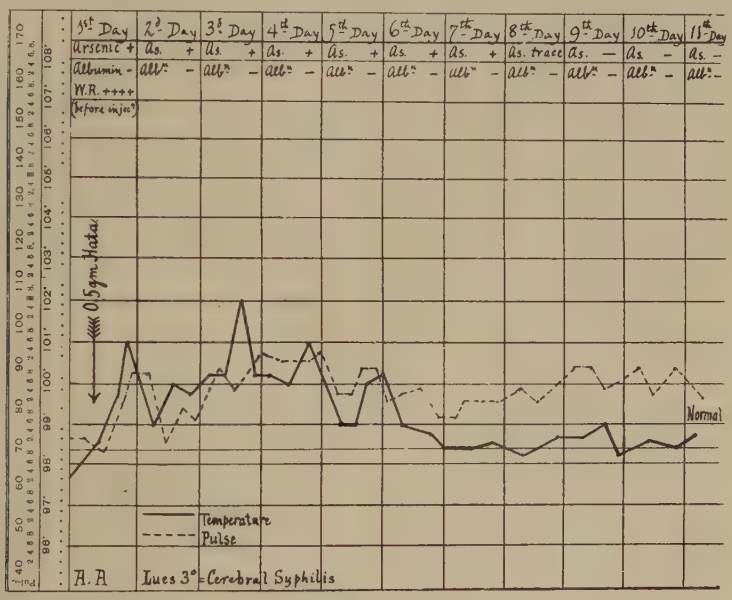


Fig. 10.

I consider this a most opportune moment to repeat a note of warning to all who are about to begin the use of this powerful remedy, as soon as it is given to the public. Certain precautions must be insisted upon:

1. No one should attempt to administer the treatment unless he has seen it given by another, more experienced. Faulty technique may cause a fatal result.

2. The remedy should not be administered to ambulant patients. Ehrlich also insists on this point, and all experience confirms the correctness of his view.

3. It should be administered only in a hospital, or sanitarium where the most careful asepsis can be observed, and where a thorough watch can be kept on the patient's condition at all times. In a private home,

with a trained nurse in charge and a physician within easy reach, it can also be given with safety. The patient should be seen every day.

4. The urine should be examined every day as to quantity, specific gravity, and as to the presence of albumin and arsenic.

5. The patient should be kept thus under close observation for at least ten days, and preferably two weeks. It is a common experience that once the patient is permitted to leave the hospital, he seldom returns for further observation.

6. We should not for one moment forget that we are dealing with a product capable of producing toxic effects, and that patients vary in their susceptibility to this and other poisons.

Briefly, we may conclude that the remedy gives evidence of being able to combat successfully conditions that remain unaffected by mercury and iodides for months and years; that while it is wonderfully effective, it must be used cautiously; certain persons show a susceptibility towards the drug, with the result that alarming symptoms may arise; these alarming symptoms disappear as soon as elimination is augmented; at no time do the patients give evidence of being "sick," even when the temperature runs above 105° F. The high temperature is due to the reaction of metabolism, caused by the absorption of the arsenic. Lastly, we have added to our therapeutics, through the immortal genius of Ehrlich, the most powerful weapon in the fight against syphilis, that civilization has ever known.

I desire to express my thanks to the members of the House Staff of the People's Hospital, for their courteous coöperation in making the daily urine examinations in all of these cases (except case III.), and in many others, which will be published at a later date. Likewise to Dr. I. M. Rottenberg and Dr. M. Rosenbaum of the Visiting Staff, for their special examinations before the treatment was administered and during the patient's stay in the hospital. Examinations for spirochetes were made by Dr. Walter J. Heimann, and the Wassermann tests were made in the laboratory of Dr. N. Kruskal.

105 East Nineteenth Street.

RECENT PROGRESS IN THE TREATMENT OF SYPHILIS.

By H. Hallopeau, M. D., of Paris, France,
Member of the Academy of Medicine.

To begin with, I shall describe step by step the curative and abortive treatment of syphilis.

Progress in Curative Treatment.—The introduction of new arsenical preparations in the therapy of syphilis was a decided advance as regards progress. In 1907 Salmon used the preparation popularly known as atoxyl, but which is in reality paraminophenylarsinate of soda, and contains 31 per cent. of arsenic. Prior to 1907, it had been proved that atoxyl had a decided action on the trypanosomes of sleeping sickness, and bearing this knowledge in mind, Salmon arrived at the opinion that it might be equally efficacious in destroying the treponemæ of syphilis. In a communication to the Biological Society, Salmon announced the results of his first attempts with atoxyl as a curative agent. The results were most encouraging, for when this medicine was administered in large hypodermic doses, it was very well tolerated and in a few days the syphilitic manifestations disappeared. Numerous cases of syphilis had been treated at the St. Louis Hospital by six injections of 0.5 grm. each. The disturbances following the injections were digestive, and though these were intense their duration was short. A number of Salmon's confrères were not so successful as he in the use of this new arsenical preparation, and to-day the record shows that 27 cases of blindness were produced by atoxyl. This untoward occurrence caused physicians to decrease the dose, and in one case ten consecutive injections of 0.05 grm. each caused blindness. Hence, the conclusion must be drawn that atoxyl contains a high degree of toxicity.

Prof. Ehrlich, after the unfortunate experiences of physicians with atoxyl, thought he had discovered a product that would have happier results. This product was called by Ehrlich arsacetine (acetyl paraaminophenylarsinate of soda) and contained 26 per cent. of arsenic. The dosage was twelve doses of 0.6 grm. each at intervals of four days, and on account of the smaller proportion of arsenic, it was hoped that there would be a diminution in the toxic action. This preparation was extensively employed in large doses in various hospitals throughout Germany, and its therapeutic action was approximately the same as was that of atoxyl, though it was believed for many months that this new preparation was an active and an inoffensive remedy for syphilis. Again the record read that many patients became suddenly blind after one injection;

hence, arsacetine must be classed with atoxyl as a preparation that is so toxic that it would be criminal not to abandon it at once.

Will the results be more fortunate from the use of the Ehrlich-Hata preparation known as "606?" This preparation (dioxydiamidoarsenobenzol) contains 41 per cent. of arsenic and should be administered in doses from 0.5 to 0.6 grm. It is claimed that all the direct manifestations of syphilis are so decidedly affected, that its action is incomparably greater than that of any other therapeutic agent; that in a few days papules disappear, ulcers cicatrize and gummata recede; that it is an infallible destroyer of treponemæ; that its effects are lasting, though at times it is necessary to give a second injection after some weeks; and furthermore, it is claimed that the problem of the cure of syphilis is solved.

Already, though this preparation has been in use only some weeks, a number of regrettable facts can be registered against its use. I do not mean by this the intense pain that is caused by intramuscular injections; an inconvenience such as this should not weigh much in the face of important results. But what I do mean are the lack of simplicity in preparing "606" before its use, and its alterations which occur rapidly; hence the necessity of making a fresh solution immediately before the injection. The procedure is as follows: In a graduate, previously sterilized, 50 c.c. are mixed with a few drops of methyl alcohol, to this 10 c.c. of distilled water are added, then slowly from 0.02 to 0.03 grm. of a soda wash are added until 0.1 grm. has been used, and finally 20 c.c. of sterilized water are used. The temperature is lowered by neutralizing the liquid with about 2 c.c. of a 1 per cent. acetic acid solution. All this takes up one hour, but despite the length of time in preparing the solution, this fact may be overlooked as well as the painful local reaction which is troublesome enough at times. The important matter, however, is the general condition of the patient after an injection, since this is weighty enough to be considered a serious impediment to the use of this new preparation. The disturbances are vomiting with profound depression, occasional disappearance of the patellar reflexes, retention of urine, paralysis of the lower limbs; and finally it may be recorded that a number of deaths have followed the injections.

Should these be considered but mere coincidences, as affirmed by the defenders of this new preparation? To begin with there should be mentioned the deaths of three out of five children to whom Wechselmann administered "606." Here we have undoubtedly the relation of cause and effect; hence, if this medicine produces in the young child such grave disorders that death results, it must be admitted that its action on the adult cannot be other than toxic. Moreover, there is to remember that it may engender in the organism latent disturbances that must be seriously considered; therefore all those patients who have submitted to this treatment should be watched with the greatest care during many weeks. The

probability of alterations in various organs should be a contraindication against repeated injections in the same patient.

It has been claimed that on account of the large dose of "606" all recurrences should be excluded as a certainty. Yet, in spite of this assertion, there have been 10 per cent. recurrences in all the cases, though only a short time has elapsed since the introduction of this new treatment. When one remembers the remarkable faculty that the treponemæ of syphilis have as regards latency, one cannot but consider the assertions, which have been made in certain quarters as to complete cures, as decidedly premature. Moreover, where recurrences take place after so short a time as has been evidenced in this treatment, the physician should not be forgetful of the occurrence of grave deuteropathies of the nerve centres, blood-vessels, viscera, and bone-tissues. Hence can it be said in all fairness that we are in possession of an agent that is definitely curative of syphilis?

Benzosulfoneparaaminophenylarsinate of soda, introduced into therapeutics by Mouneyrat, more than a year before the discovery of "606," and which is known by the name of hectine, is free from all dangers. Observations made by Balzès and Milian, as well as by myself, have resulted in convincing me that in a moderate dose of 0.2 grm. a day, repeated regularly during three or four weeks, this remedy is efficacious for those manifestations of syphilis which have resisted the action of mercury. Of such cases one of Gaucher's patients showed the remarkable effects of hectine. Intolerance is unknown; and, on account of this, Milian at the present moment is making researches to ascertain whether the dose of hectine can be increased with safety to the patient, so that a therapeutic action comparable to that of "606" may be achieved. The result of these facts indicates that we are progressing towards finding a cure for acquired syphilis, and that having abandoned atoxyl and arsacetine, the near future must decide between hectine and "606."

Progress in Abortive Treatment.—In this connection no doubts remain in my mind. The time which has elapsed since I made my first experiments—twenty-two months for one and fifteen months for the other two—has convinced me that appropriate local treatment of the chancre, instituted within thirty days of its appearance, prevents a patient from having any secondary manifestations. I, myself, have carefully studied fourteen cases, and to these should be added those of Fouquet, Guiard, Maisonneuve, Mariotti, and Moniez. This treatment by hectine is the outcome of a new interpretation of the primary lesions. According to my observation the clinical facts have shown that syphilis is not, as is usually thought, a general infection from the time of the appearance of the chancre, but a local infection limited to the area in which the chancre is situated, to the tissues which surround it, and to the lymphatics. This localization lasts throughout the forty-two days of incubation. If during this time any treponemæ penetrate into the general circulation, their number is very small, and, moreover, their virulent activity is decidedly feeble.

Hence a thorough local treatment ought to be the right thing in this disease, and ought to be able to nip it in the bud: surmises which have been verified as truisms in my practice.

I employ hectine in the daily dose of 0.2 grm., dissolved in 1 c.c. of sterilized water. In case the chancre is penile, the needle is introduced, the first two or three times, into the tissues immediately contiguous to the chancre. This produces at once a slight elevation, which, however, disappears at the end of twenty-four hours. The pain which occurs after the first injections is quite severe, but can be abated by cold applications or cold local bathing. The later injections are not followed by this untoward symptom, as the tissues become accustomed to this sort of interference. Thirty days later the injections are repeated.

Fouquet, who treated two patients by giving injections of hectine, reports that both were cured, one after five, and the other after eight injections. In one of my own cases in the Municipal Hospital of Nanterre, fifteen injections prevented the appearance of secondary manifestations. Thus if a larger number of injections are given, it is merely done to make the success of this medication more complete. The chancre is cured by hectine in a few days, the lymphatic glands resume their normal size; but what should be specially emphasized is that secondary manifestations do not appear. The Wassermann reaction is generally negative shortly after this treatment has been instituted, but at times it is necessary to wait for this result until several months have elapsed. In women the needle is introduced into the cutaneous border of the labium majorum and then pushed in beyond the mucous membrane.

I employ exclusively hectine, since the only mercurial preparation, which is well tolerated in connection with this medication, is the oxycyanide, which has been given by Mariotti with good results in doses of 0.002 grm. On the other hand, Moniez has used atoxyl without any bad results; however, to generalize the use of this arsenical preparation would be inadvisable.

The therapeutic method which is advocated in this paper is an abortive one, since there results a complete destruction of the treponemæ in the initial lesion. To reach the few treponemæ, which get into the circulation before the chancre is healed, I advocate adding to the local treatment twenty subcutaneous gluteal injections of 2 c.c. each of a 1 per cent. benzoate of mercury, according to Gaucher's formula. The success of hectine is invariable, and up to the present time no case of failure has been recorded. The persistence of a positive Wassermann reaction in certain cases is of no great moment as an indication of the presence of treponemæ, as I have seen it negative at the end of some months in cases in which the treatment was not repeated.

Local treatment by means of "606" is out of the question, since the dose is altogether too large to be injected around a chancre; hence, hectine is to be preferred, for it can be used locally and is never followed by secondary symptoms. If hectine were more generally used there would be no need of "606," because there would no longer be treponemæ in the organism.

GIANT CELLS IN SYPHILIS.

By JOHN A. FORDYCE, M. D., of New York,
Professor of Dermatology and Syphilology, University and Bellevue Hospital Medical College, New York.

According to our cytological classification multinucleate structures of both physiological and pathological origin are included under the term giant cell. A discussion in extenso of the various theories relative to the formation and function of these bodies is beyond the scope of this paper, the chief aim of which is to demonstrate that the majority if not all of the giant cells met with in cutaneous syphilis owe their origin to vascular changes.

To recapitulate some of the more prominent views on the formation of giant cells in general, it is held (1) that they are produced by the coalescence of several cells; (2) that they result from nuclear division of one or more cells, and (3) that they owe their origin to transformed vessels. To differentiate between the types arising from cell division and those resulting from cell fusion, the term syncitium is often limited to the structures arising from multiplication of nuclei without subsequent division of cell body, while plasmodium is descriptive of the forms due to fusion of several cells. An example of the former process is found in the syncitial tissue of the chorionic villi, and of the latter in the phagocytic eosinophiles and macrophages which may form a plasmodium about bacteria, lose their identity as single cells but later may again separate and become free. Morphologically giant cells are further classified into myeloid with a central or equal distribution of nuclei and Langhans when the arrangement is polar or peripheral. As to the mode of nuclear division, both mitosis and amitosis may take place, the nuclei in the syncitium of the chorion, for instance, dividing by the latter process, and it is believed by the majority of observers that in pathological giant cells, while the nuclei in the early stages multiply by mitosis, later amitotic division takes place.

Giant cell formation is probably not peculiar to any type of cell and as their progenitors are found in leucocytes, plasma, endothelial as well as epithelial and connective tissue cells, a liberal interpretation as to their origin is only logical. When we consider the variety of conditions under which multinucleate forms occur, their presence can perhaps best be explained on the assumption of a tissue reaction, and that different cells when subjected to abnormal conditions, such as occurs when nutrition is impaired from mechanical or chemical cause, or when stimulation takes

place from the presence of an organism or foreign body, may give rise to these structures.

Pathologically, giant cells occur in their most typical form in tuberculosis, where the concensus of opinion appears to be in favor of their endothelial origin. While endothelial cells are phagocytic for bacteria it has been shown that they also react to toxins, as of the tubercle bacillus, for example, which are likewise capable of inciting them to proliferation. This is illustrated in tuberculides where giant cells are met with in the subcutaneous adipose tissue or more superficially in the corium about necrotic areas. In blastomycosis they probably arise from vascular endothelium,

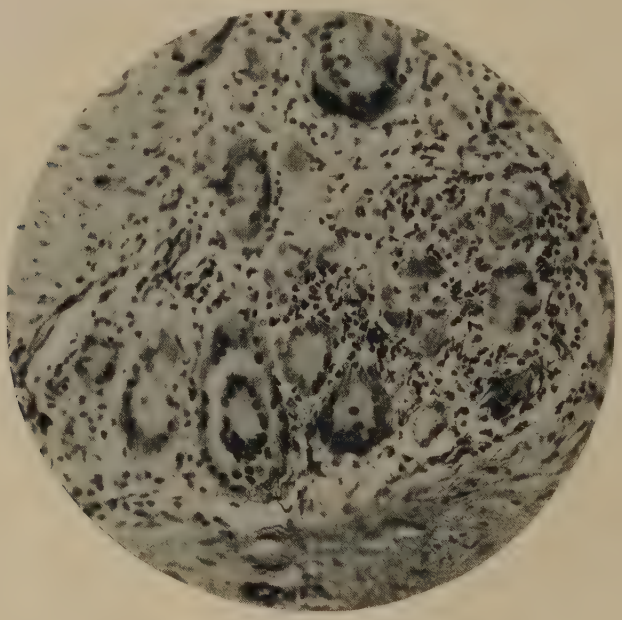


Fig. 1. TUBERCULAR SYPHILIDE.

Spencer ¼ in., Zeiss Proj. Oc. 2.

Section through an area containing a group of capillaries transferred into giant cells.

adventitial cells and leucocytes, but where they occur between the rete cells, the wandering cells offer the best explanation for their genesis, unless we admit ameboid properties of these multinuclear phagocytes. In certain types of sarcoma giant cells are also numerous, especially in myeloma, in which they differ from those of inflammatory conditions in having their nuclei distributed throughout the cell body as in myeloplaxes. They are not at all uncommon in epithelial or endothelial tumors, especially in connection with degenerating areas and often about epithelial pearls. In these growths it is probable that leucocytes as well as endothelial and epithelial cells contribute to their formation.

In syphilis giant cells play only a secondary rôle and are chiefly of

interest because of the difficulties they present in a differential diagnosis from other infective granulomata, especially tuberculosis, and on account of their possible influence on treatment. Although many minor distinctions are made upon which to base a diagnosis between a tuberculous and a luetic lesion, in the majority of cases from the histology alone it is impossible to say to which class of infections the specimen belongs.

Giant cells are not pathognomonic of any stage of syphilis. With the exception of the roseola and mucous patches they have been reported in

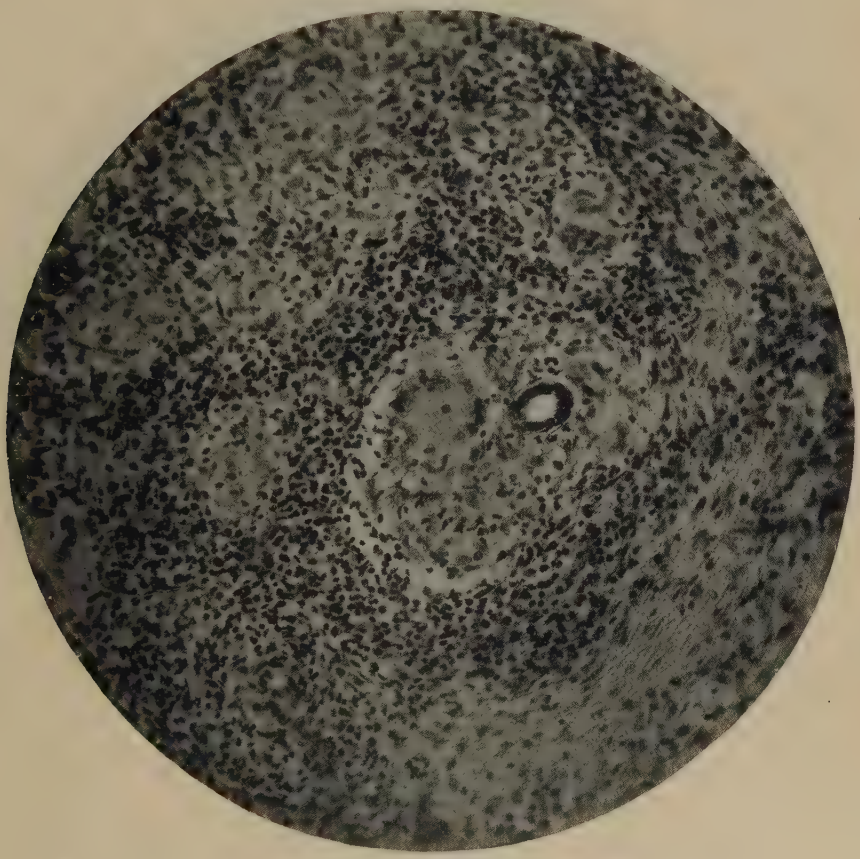


Fig. 2. TUBERCULAR SYPHILIDE.

Zeiss ¼ in., Comp. Oc. 4.

Showing vessels with proliferated endothelium and production of giant cells.

all other lesions of the disease. The writer's material does not verify their finding in initial lesions, but Unna reports them in the persistent nodules which often remain at the site of such lesions. They are more constantly encountered in the papular lesions, especially the small type or lichen syphiliticus and in the late secondary nodular or serpigenous

lesions. The view that they result from the fusion of plasma cells is still held by many histopathologists, and while not an untenable one, there appears to the writer more corroborative evidence in favor of their vascular origin.

The small lichenoid syphilide, owing to its localization about the hair follicle and the giant cells, which contribute so largely to the histological picture, is practically indistinguishable from that of lichen scrofulosorum.

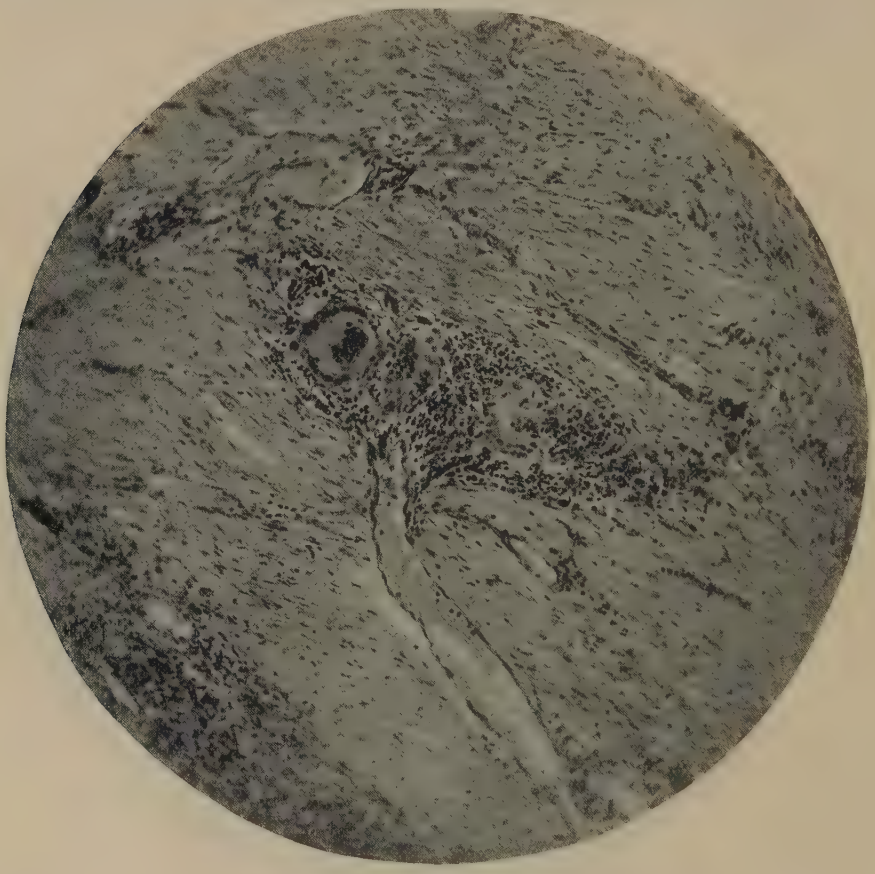


Fig. 3. SERPIGINOUS SYPHILIDE.

Zeiss 8 mm., C. O. 4.

Giant cell formation and thrombosis of vessels in a serpiginous lesion.

The more frequent occurrence of giant cells in this type of syphilitic papule might possibly find an explanation in the richer vascular distribution about the pilo-sebaceous apparatus, and the operation of several factors over a limited area, such as the endothelial stimulation occasioned by the spirochætæ and the dense cellular infiltration confined to the follicular vessels. The latter interferes with nutrition and results in

partial or complete thrombosis of the capillaries which on cross section may simulate giant cells. (Fig. 1) illustrates a portion from such a lesion. Of the vast number of capillaries present in the early stages only a few dilated ones remain. The majority are either thrombosed or their former site is marked by a group of irregularly disposed nuclei or giant cell structures of the Langhans type which have probably arisen from a multiplication of endothelial cells.

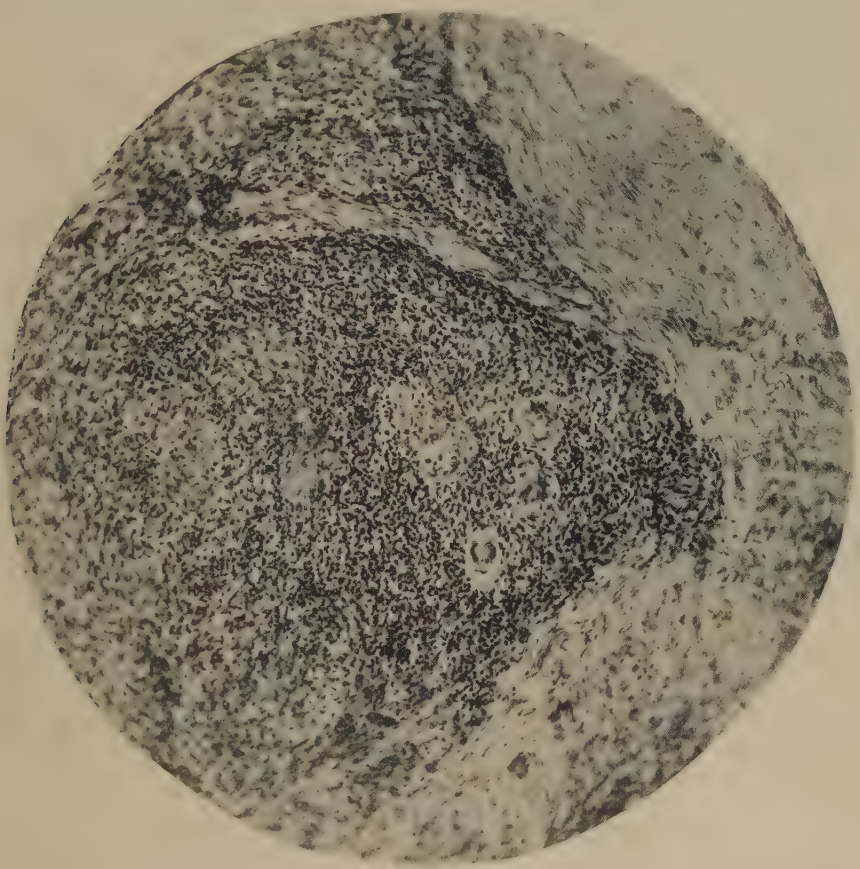


Fig. 4. LICHEN SYPHILITICUS.

Zeiss 8 mm., C. O. 4.

A focus from periphery of lesion showing giant-cell formation.

In the nodular lesion (Fig. 2) the microscopical picture is frequently that of a diffuse infiltration of the corium showing alternate light and dark areas. This mottling is due to changes which the vessels have undergone, the light areas representing all gradations from a choked up lumen with swollen and proliferating cells to distinct giant cell formation, while the dark ones are made up of the inflammatory infiltration. One

frequently notes also a variable number of endothelial nuclei irregularly disposed which may, perhaps, be looked upon as a transition stage.

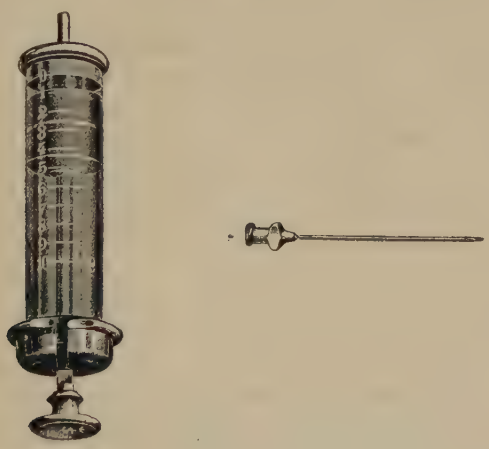
The histology of serpiginous lesions as illustrated by (Fig. 3) is very suggestive of the relation between the vessels and the clinical characteristics of this type of eruption. These changes have suggested to the writer that the extension of the serpiginous lesion may be due to a progressive thrombosis of the vessels. Cross section of the tortuous portions of the latter shows typical giant cell formation with proliferation of the endothelium, while tangential section shows the lumen occluded by a thrombus. This view is further supported by (Fig. 4), from a section in which several similar foci were almost exclusively made up of giant cells, varying in size and form, with single or multiple rows of nuclei after the Langhans type. The latter lesions had persisted for months in spite of most vigorous antisyphilitic treatment. Occluded or transformed vessels like the foregoing offer a plausible explanation for the failure of these and similar luetic lesions to yield to specific treatment, as it is obviously impossible for the drug to reach the morbid process. Those lesions of syphilis in which the vessel changes are most pronounced are the least amenable to mercury alone, as is illustrated in the obstinacy of the late serpigenous and gummatous lesions, but when this drug is combined with potassium iodide a very rapid therapeutic action is noted. The use of this mixed treatment, which is supported by clinical observation, may be explained by the action of the latter remedy because of its well-known property in resolving an inflammatory infiltration and possibly rendering the vessels which were previously occluded pervious to the action of mercury, the real agent in bringing about the destruction of the spirochætæ.

PERSONAL OBSERVATIONS WITH THE EHRLICH-HATA ("606") REMEDY.

By B. C. Corbus, M. D., of Chicago,
Adjunct Professor of Genito-Urinary Diseases, College of Physicians and Surgeons, Medical Department, University of Illinois.

In a communication dated October 25th, 1910, Prof. Ehrlich says that so far forty thousand ampoules have been placed in the hands of the medical profession and that the new specific has passed the experimental stage, its therapeutic value being well established.

It seems almost incredible that a disease which has cursed humanity for ages should have its door unlocked in seven years, for it is but a short time since the possibility of animal experimentation with syphilis



on monkeys was announced, which led in turn to the discovery of the spirochæta pallida as the causative factor, followed two years later by the Wassermann test; and now, three years later we have a specific remedy in the dioxidiamidoarsenobenzol, or "606," which was discovered by Ehrlich and Hata, and announced to the profession by Alt, Schreiber, and Wechselmann (June, 1910).

Even if time should prove that this substance is not an absolute specific for syphilis, we can be well satisfied with our present results, for here we have the best aid yet available to combat this dreaded disease.

We have in "606" a substance that has been prepared on a scientific

basis, through years of careful research and experiments: a substance that was carefully tried out upon animals and trusted co-workers before it was given over to the general profession.

As it was not possible to perfect a serum therapy for syphilis, Ehrlich set about to find certain chemical substances that were particularly attracted to certain parasites, these he called parasitotropic. Being poisons and capable of injuring cells of organs, these substances are also organotropic and their curative value in parasitic diseases depends on the existence of a proper relation between the parasitotropic and the organotropic properties. After many experiments and many failures, Ehrlich finally succeeded in preparing dioxidiamidoarsenobenzol for the cure of syphilis.

The parasitotropic power of this remedy, if used in the proper dosage, greatly overshadows the organotropic, and so far in fourteen thousand cases reported there have been no evil results or organotropic disturbances which could fairly be attributed to the Arsenobenzol.

Ehrlich believes from the results of animal experiments, that the most efficient method of combating this disease is by his "Therapia Sterilisans Magna;" that is, by killing as many spirochætes as possible by one maximum dose, in the same way that malaria is combated by exceedingly large doses of quinine in a short interval. We all know that by giving small doses the organism may become accustomed to the substance as shown by Dr. Marks, Ehrlich's first assistant, in the action of "606" on the trypanosomes.

Indications and Precautions.—At the present time, "606" is indicated in every case of active spirochætal infection, but most particularly in all cases of primary, secondary, and tertiary lues with external manifestations.

In visceral and cerebro-spinal syphilis, it should be used with extreme caution depending upon the condition of the patient.

In aortic aneurism of syphilitic origin, also, extreme caution should be used.

Dosage.—The drug has been described as a sulphur-yellow powder. It is put up in vacuum ampoules, as the drug is manufactured entirely under nitrogen, and it must be prepared immediately before using.

The dose depends upon the method of administration, the length and severity of infection, and upon the age of the patient.

Children—0.002 grams for babies five to six weeks old have been given repeatedly intramuscularly, but here of course the dose must be proportional. Ehrlich discourages the administration of "606" to children under the age of one year.

Women.—The average dose intramuscularly is from 0.45 to 0.6 grams, while by the combined method 0.4 to 0.5 grams intravenously may be safely followed by 0.45 to 0.6 grams into the glutæus depending on the weight of the patient.

Men.—The average intramuscular dose is 0.6 grams, but by the combined method 0.5 to 0.6 grams intravenously followed by 0.6 grams intramuscularly is considered safe in well-nourished patients.

If we expect to accomplish a maximum effect and adhere to Ehrlich's theory of "Therapia Sterilisans Magna," it is necessary to give as large a dose as possible. However, in latent syphilis and cerebro-spinal syphilis where the infection is reduced to a minimum, the dose may also be reduced.

Administration.—The many methods of administering the remedy are indeed confusing. The original technique of Alt, of intramuscular injections, as recommended by Ehrlich, and practised by Lesser in Berlin at the Charité, and by myself in this country is by far the simplest.

The neutral suspension, as employed by Wechselmann, is difficult to prepare, is apt to cause complications, and is far slower of absorption; the method of Kromayer is not difficult to follow, but I have had no personal experience with it. The numerous other methods are practically only slight modifications of either the neutral suspension or the alkaline solution methods.

The most rapid in its action is the method of giving "606" by intravenous injection suggested by E. Schreiber, though it is followed at times by vomiting and a considerable rise of temperature. These conditions are not produced by the substance, but by endo-toxins suddenly liberated into the blood stream from the killed spirochætes.

For a more comprehensive method of taking up the management of the different kinds of syphilis, the following classification is used:

(1) Congenital syphilis. a—Scelerotic.
(2) Primary affections. b—Erosive.
(3) Early secondary.
(4) Late secondary.
(5) Tertiary.

Congenital Syphilis.—While I have had no personal experience with "606" in hereditary syphilis, I have seen numerous cases treated in both Wechselmann's and Lesser's clinics. The dose employed was usually 0.002 grams. All babies that I saw treated showed a wonderful improvement in four to five days. Patients covered with macular eruptions cleared in five to six days. Karl Taege's unique experiment may be of interest in this connection.

A woman pregnant at term exhibited mucous patches, condylomas, and spirochætes. The child was born extremely pale, weak and sickly. It did not cry, but lay in an apathetic state and took the breast poorly. No characteristic signs of syphilis appeared until the eighth day, when numerous lesions of pemphigus appeared on the soles of the feet and at the same time syphilitic paronchia on both hands. These lesions tending to spread, the mother was injected into each buttock with 0.03 grams of Ehrlich's "606" in sterile water. On the third day the woman complained

of pain, on the fourth day a reddish exanthem appeared on the buttocks, and on the fifth day a headache developed. Three days after the injection the lesions began to fade rapidly and the spirochætes disappeared. The child showed increased spread of the lesion for two days following the mother's treatment. The third day it showed rapid clearing up of the symptoms and by the fifth day the pemphigus and the paronychia had disappeared, the grayish pallor had given place to a healthy tint, the child was no longer apathetic, but cried lustily and took the breast greedily. Ten days later the child was well and free from symptoms.

An explanation of the production of this remarkable result is difficult to find. That the "606" compound was not transmitted to the child through the mother's milk was shown by the fact that this milk contained no trace of the arsenic. Ehrlich himself explains it by the theory that the sudden destruction of the spirochætes set free a large amount of endotoxins which excite the productions of antitoxins, and the latter are then transmitted through the mother's milk to the child with curative effect. However this may be, the sudden clearing up of the symptoms in the child did follow the use of the "606" on the mother, and this result may offer a new and improved method for treating syphilitic infants. Ehrlich especially warns against injecting his remedy directly into small infants, not from any toxic quality in the remedy itself but from the large amount of endotoxins liberated in the child's system from the destruction of the many spirochætes.

Herxheimer and Michaelis both report post mortem examinations on babies that had died following injections of "606;" they attribute the death as not due to the direct action of the substance, but to the action of the endotoxins produced so suddenly as to absolutely annihilate the little patients. In none of the organs, only excepting the lungs, could any spirochætes be found, whereas only a few degenerated forms were found in the latter organs.

Primary Lesions.—In an article in the *Journal of the American Medical Association* in the fall of 1908, I advocated the total excision of the primary lesions. In doing this I was carrying out the teachings of Neisser and Jadassohn, knowing full well that I could not abort the infection, but believing that I could attenuate it by removing in mass the first known collection of spirochætes. In a recent article that appeared in the same journal, I cited numerous cases that were treated in this manner, always beginning treatment immediately after excision was performed. In all of these cases in which treatment has been carried out as directed the cure was rapid under mercury and iodide treatment.

With "606," I believe it is possible to do the same thing only in a much shorter time.

The most successful and ideal case for treatment is the primary lesion with an early diagnosis made before the system has been invaded to any considerable extent by spirochætes.

With the dark field illuminator and the india ink stain, the task of making a diagnosis is not difficult, and it is imperative if we wish to make the most out of our treatment and to carry into effect Ehrlich's theory of "Therapia Sterilisans Magna." To wait for secondaries, is like closing a door after the flies are all inside.

In this class of cases, Ehrlich himself suggests that first the primary lesion be disposed of either by excision or the cautery, then immediately an intravenous injection of "606" is to be given, followed in five days by the intramuscular injection of a weak alkaline solution of the specific.

The first dose will act immediately as a mighty sword, killing thousands of spirochætes, but it will soon be eliminated. The second dose will act as a skirmish line in the rear and will effectually take care of the straggling spirochætes that chance to remain behind. This is Ehrlich's theory of "Therapia Sterilisans Magna" and this is what is meant by the statement that he can cure syphilis in one single dose, namely, 0.5 or 0.6 grams (entirely) intravenously followed in five days by 0.5 to 0.6 grams intramuscularly.

Of course this is only possible in cases in which the diagnosis is made before the Wassermann shows a systemic invasion.

The procedure, however, is not limited to primary cases, for it is our duty to carry out the same technique, in all primary, secondary and tertiary infections when we believe that the infection is severe enough to warrant such a procedure.

In reference to the erosive and scelerotic chancre, the latter, on account of the severe endarteritis present, offers a most resisting wall for the protection of the spirochætes from the substance, and it should, therefore, be excised in every case where it is possible without undue loss of tissue.

So firm is my belief, both from personal experience and from observation, that if it were possible to have all our cases come for treatment at this time, I am convinced syphilis should be eradicated forever in the above manner, but unfortunately we must treat the patient that has gone before—namely the one carrying the later forms of disease.

Early Secondaries.—It is this class of cases that we see most often. Here the infectious organism has gone through the system. Where we had relatively few organisms in the primary stage, we now have millions and the possibility of killing every spirochæte in one or two doses (namely an intravenous and intermuscular) is doubtful. However, we must place the patient under treatment at the earliest possible moment, for every day means continued growth of the spirochætes and just that many more to exterminate. By injecting the patients as soon as a diagnosis is made, I believe from personal experience that it is possible, to so sterilize them at once, that they are rendered safe members of their families and communities. That it is possible to completely destroy the organisms in

manifest lesions in from twenty-four to forty-eight hours has been repeatedly reported by many observers.

Late Secondaries.—The most infectious and discouraged patients are those that reach their second, third, and fourth year with the disease still manifest. In one instance, I found the organism in mucous patches eight and one-half years after the primary infection.

In this class of cases it may be possible to dislodge the spirochætes, as it were, from the glandular, osseous, or any other tissue they may happen to be located in by a preliminary treatment with potassium iodide. This is the method that I am following out at the present time and soon I expect to put them through the same course of treatment as the more acute cases.

Tertiary.—It is this class of cases that responds most beautifully to the specific. This is due, in the opinion of Ehrlich, to the fact that there are a large number of antibodies in the circulation and one injection stimulates the organism in an emphatic manner. It may also be explained on the hypothesis that the strain of spirochætes present is well-nigh exhausted in virulence and that a little of the specific acts in a far-reaching manner.

In Wechselmann's clinic in the Virchow Krankenhaus, and in Lesser's clinic in the Charité, I have seen most beautiful results, and in one case of my own series a gumma involving the nasal bones had completely healed in seven days.

As my observation and personal experience with dioxidiamidoarsenobenzol is confined entirely to the manifest external signs of syphilis, I am at present not able to form any opinion in regard to its value in visceral syphilis and in syphilis of the nervous system. In fact, Prof. Ehrlich expressly requests that the substance be used at first only upon early cases, knowing full well the danger of complications in patients who are already debilitated by disease.

However, the substance has been tried on every phase of the disease. Almost all of the investigators have treated a limited number of tabetics, but the results in these were variable. All agree that in paresis the substance should be given as soon as the diagnosis is made.

Excepting optic atrophy the substance has been used in lesions of the eye by Professor von Grosz, head of the first Ophthalmological Clinic of the University of Budapest. He has treated successfully by means of "606," 14 cases of syphilitic ocular lesions: 1 ulcer of the cornea, 3 iritis, 1 iridokeratitis, 1 scleritis, 2 chorioretinitis, 6 keratitis. He furthermore declares that the existence of syphilitic ocular lesions should not be considered a contraindication in treatment by this method.

In aortic aneurysm of luetic origin unless the diagnosis is made extremely early, we had at present better confine the treatment to mercury and the iodides.

Results.—All observers agree that the immediate results are sur-

prisingly favorable. I believe from observations on my thirty cases treated to date, that it is possible to do more with one injection in four days than one can accomplish in six to seven months with continuous mercury treatment. As compared to all other forms of treatment, in primary, secondary, and tertiary cases, in the absence of fundus changes and of kidney and cardio-vascular disease, it is the treatment that is demanded as the best means of combating the disease early.

In all my cases using the intramuscular method of Alt and Lesser, I have had no complication. It may be necessary to employ later some form of mercury treatment in addition, but even then we know we have our patients already well on the highway to recovery.

The question arises, What are the remote effects and how can we tell whether a patient is cured?

Up to the present writing, with fourteen thousand cases reported, the observations extending over a period of twelve months, there have been no serious after-effects in competent hands.

As we are dependent entirely upon the Wassermann examination as the only method now at our command of sufficient accuracy to show when a given patient is cured, we will have to be content to wait until numerous statistics are available before we can draw conclusions.

In the meantime we must strive to be exact in diagnosis, using laboratory means when in the least doubt and employing above all things, absolute accuracy and thoroughness in the technique of administering the substance.

THE PUBLIC AND SYPHILIS.

By Isadore Dyer, Ph.B., M. D., of New Orleans,
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With the pandemic spread of syphilis over continental Europe in the sixteenth century, the first public notice of the "Italian Disease" probably was effected. No doubt earlier epidemics occurred and may have attracted attention, but syphilis as such was not isolated and recognized sufficiently to be remarked. In Scotland particularly, syphilis made such extensive ravages that its progress in households and community was comparable to the plague.

Such a wave of infection has not occurred since, and to-day it is not at all likely, since syphilis has become so generally known and so generally prevalent that few countries of the world are virgin to this disease.

While the source of origin of syphilis is still unknown, there is strong opinion based upon Biblical references placing the disease among the Levitical types, while on another hand the pre-Columbianites have presented many arguments and much evidence to show syphilis an early American disease.

The facts remain that the disease has spread systematically along the avenues of civilization and colonization and that the least affected are those districts and countries most remote from large centres of population.

The efforts to treat syphilis, together with the natural progress of the disease to self-limitation, have resulted in a general immunization in those countries where the disease has for long prevailed. At the present time the profound evidences of syphilis occur in country districts and in new territories where the disease is more recent.

The by-effects, however, as expressed in late nervous affections and in the evidence of hereditary influence are constantly on the increase, and the insane asylums everywhere are burdened with the victims of this disease, either suffering the penalty of their own sins or the transgressions of their ancestors.

The estimate of the prevalence of syphilis can only be comparative, as any statistics must be inadequate and inaccurate with a condition which is so often concealed by the physician who may have occasion to treat it.

Insurance companies have contributed largely to the study of the incidence of syphilis and its relation to longevity; and in the past twenty-five years the actuary tables of these companies have been almost the

only reliable basis for a study of syphilis in relation to the economics of human life as compared with other diseases.

In the absence of any known basis of estimate for the occurrence of syphilis, certain syphilographers have drawn conclusions from the limited observations of those who have made records of such and who most often meet the disease.

Some years ago one of these (the late Dr. Hyde) estimated that about 18 per cent. of the people of the United States were syphilized. Accepting this estimate, hypothetically only, the figuring is appalling enough to demand a wider interest and broader knowledge of syphilis among the public than has hitherto obtained.

Until quite recent years, syphilis has been a subject tabooed in the periodical and daily press, as well as in circles of people otherwise educated. Latterly a more general interest has been excited by the legislation undertaken in a few States, and by the medical discussion of the disease with reference to its treatment and its relation to sociological questions.

Although a number of diseases far less virulent have been listed among the quarantinable diseases, syphilis has never been entertained from that point of view, in spite of the fact that to this factor alone is due a larger proportion of defectives, in and out of the insane asylums, than to any other cause.

The habit of relegating syphilis to the venereal group and classing it as a vicious condition has prevented a free discussion of its importance to society. With the recent advanced ideas among the reading public, and with the improved educational basis in the minds of such, the field for instruction is ripe and the present generation should be made to know all that syphilis means.

Several of the United States have already legislated regarding the marriageability of syphilitics and eugenists have urged the protection of the offspring of such persons by radical procedures. There is a middle ground, however, and based upon the known curability of the disease. With the present laboratory technique available, no mistake should be made by those who have ever had syphilis, and a proper safeguard of society could be provided if the knowledge of these things were made common. A Wassermann test is obtainable almost everywhere to-day and its evidence is always important enough to stay the young man engaged in the pursuit of matrimony.

It is a crying disgrace to modern methods prevalent in hospital and clinic practice that syphilis is not made a more important subject of care, so far as education and treatment are concerned. Even with the presumptive estimate that only one in fifty persons exposed to syphilis contracts the disease, it remains that some twenty-five per cent. of innocent persons acquire the disease outside of sexual relations, and those twenty-five in each hundred should be protected.

In such a brief review of the relation of the public to syphilis it is impossible to go far afield, but a summary of this topic might be summitted for medical men and others to reflect over.

Syphilis is a disease of long standing and is a part of the practice of every physician of to-day. Ignorance prevails in and out of the profession as to the possibilities in its effects and in its relief.

If the public knew more about syphilis, there would be less of it.

Health boards everywhere should distribute systematic information regarding the dangers of syphilis and its methods of spread, as well as concerning its evidences and concerning its effects.

Hospital authorities and physicians connected with eleemosynary institutions should provide more indoor facilities for syphilis in its acute stages so as to minimize the possibilities of infection of others.

The United States Government should make syphilis a quarantinable disease, and as soon as practicable local health authorities should endeavor to make syphilis a reportable disease.

We are all striving to make a saner world, and it is constantly brought to the intelligence of thinking men in all fields of humanitarian, sociological, and altruistic operation, that the more knowledge we may spread the more co-workers in our fields will develop; and though no Utopia may be consummated, the need of correction will grow less and less with the increased knowledge of the evils and their shadows in the vale of mortality.

SYPHILIS AND PULMONARY TUBERCULOSIS.

By Robert H. Babcock, M. D., LL.D., of Chicago.

Physicians have long recognized the comparative frequency with which disease of the lungs develops in persons showing luetic symptoms, or having a history of syphilitic infection years earlier. The question of special interest in those cases showing ulceration and other signs of phthisis was whether pulmonary syphilis could and actually did produce destruction of the lung parenchyma, or was there an added tuberculosis to which the extensive lung changes could be ascribed. In contrast to these cases are others in which pulmonary tuberculosis exists and is recognized as the conspicuous pathological feature, but in which either from the anamnesis or from the anomalous behavior of the disease, the query arises as to the possibility of a combined luetic infection that is responsible for the development of the tuberculosis and for its more or less peculiar course.

Relative to the former class of cases it may be stated, that the consensus of pathologists and clinicians seems to be that pulmonary syphilis alone does not lead to softening and excavation, and that when such changes occur they are the result of a superimposed tuberculosis. With reference to the latter diagnostic dilemma, clinicians until recently have been compelled to rely on the discovery of stigmata of lues or on the therapeutic test, mercury and iodides. Fortunately, we now possess in the Wassermann reaction a reliable means of diagnosis, and in suspected cases are able to institute a proper, energetic therapy before the disease has progressed to lung destruction.

As to the effect of the association of these two infections it would be quite natural to suppose this would be disastrous, but strangely enough observations and opinions on this point seem conflicting. There are some—Pourtalis, Abrahams, and Ross—who think syphilis exerts a retarding and, in some cases, even a curative influence over the tuberculosis, while others hold that pulmonary tuberculosis is distinctly aggravated by its association with lues. Cases sustaining both contentions are to be found in the literature.

Thus R. Abrahams and F. W. Ross have both reported instances of a man who in the incipient or early stage of pulmonary tuberculosis acquired a chancre and who thereafter showed marked improvement in their lung condition, and ultimately recovered. On the other hand, Stieffel recorded the case of a woman in advanced consumption, who became in-

fected with syphilis and being unable to endure specific medication rapidly succumbed.

The foregoing cases then raise the interesting question: Is the effect, whether injurious or benign, dependent on the sequence of events as regards the acquisition of the two infections? That is, is the ultimate outcome dependent on which disease is primary and which is secondary. If, as suggested by Pourtalis, there is a natural antagonism between the germ of tuberculosis and that of syphilis, then the acquisition of a chancre by a tuberculous individual ought, under all circumstances, to be more or less salutary, which as shown by Stieffel's case is not the fact.

Accordingly, when we come to analyze the reported cases of conjoined lues and tuberculosis, we discover that the effect depends largely on the stage of the primary infection. Thus, if an individual acquire syphilis in the incipient stage of his pulmonary tuberculosis, or at least before his lungs show signs of advanced disease, and before his general health has suffered greatly, then the influence of the second, that is, the luetic infection may not be disastrous, but may actually retard the advance of the tuberculosis. In other words, the syphilitic infection added to pulmonary tuberculosis, when the latter is advanced, will probably prove most unfortunate and hasten the downward course of the primary disease.

How is it now as regards the development of pulmonary tuberculosis in a person already infected with syphilis? The course of events now is reversed, for in the active stage of the lues, that is, in the initial or secondary stage, the addition of tuberculosis seems to prove disastrous, as the tuberculosis of the lungs makes rapid progress. If, on the contrary, pulmonary tuberculosis makes its appearance during the late stage of syphilis, it is likely to pursue a slow course, although no actual curative influence on the part of the lues is apparent.

From the foregoing facts we may conclude that when a consumptive is already much reduced by the mixed infection of advanced phthisis, his constitution is too greatly undermined to endure the addition of still another infectious process. He is, moreover, in no condition to bear a vigorous antisyphilitic medication. When, on the contrary, a person in the third stage of lues becomes smitten also with tuberculosis, his lungs resist the destructive tendency of the latter process because probably of the tendency to fibrosis manifested in the late period of lues. In many cases the general health does not seem seriously impaired in this stage, or at all events so reduced as to render it incapable of offering some degree of resistence to the tuberculosis. We can understand also why syphilis and tuberculosis, when both are in the early stage, should prove so serious an affair. The individual in the primary or secondary stage of lues has not yet developed sufficient antibodies to resist the spirochæta pallida as in the late stage, and hence the addition of the tuberculous infection only helps to overpower his resistance. But it is difficult to explain those instances of marked improvement following the addition of syphilis to a

previously existing, yet incipient or still early pulmonary tuberculosis. It may be conjectured that either one or possibly both strains of organisms were not especially virulent and their antibodies were capable of exerting some mutually counteracting influence. However this may be, one would hesitate to advise a tuberculous patient, still in the early stage of his disease, to contract a chancre in the prospect of its favorably affecting his original infection.

Only a few words need be said as to treatment of these combined cases in whatever stage. Experience has shown that the iodides are not well born since they undoubtedly tend to hasten the softening of the tuberculous foci.

The new remedy, "606," does not seem to have been given an extensive trial in cases of the kind here considered, but, so far as the writer has ascertained, promises well. A remarkable improvement in general nutrition follows its injection, and hence the remedy ought to affect favorably all cases in which the patient is not too greatly reduced or the lung destruction not too great. Complications as nephritis, arteriosclerosis and myocarditis, all of which are sometimes seen in these doubly afflicted individuals, would contra-indicate the employment of the remedy.

All cases which for one reason or another cannot be subjected to "606" should receive, in the writer's opinion, an energetic mercurial treatment. This is true especially for all patients who are not too much reduced. In such, mercury should be tried, but cautionsly, until its effect on general nutrition is determined. In the experience of the writer the conjoined use of inunctions and subcutaneous injections has given excellent results and this combination is recommended, therefore, when Oertel's remedy is not available.

SYPHILIS AS A CAUSE OF PAUPERISM.

By A. Ravogli, M. D., of Cincinnati.

We understand with Robert Hunter[1] a pauper to be one who depends upon public or private charity for sustenance. Paupers must be included among those suffering poverty, but poverty is a much broader term than pauperism. In order that a man may be able to work and provide for his family he must have a high degree of physical efficiency. When a man cannot retain his physical efficiency, he must degenerate. Living in poverty for any length of time means a loss of power, which renders the man unable to work; an unfortunate condition which has as its ultimate result pauperism. When a man has become infected with a disease which takes the vitality and energy out of him, he finds himself discouraged in the pursuit of his calling; he suffers mentally and physically, and becomes unable to perform work.

The man without means and without the possibility of earning his living, begins to drown his sufferings in alcohol, or to drive them away with morphine, or with cocaine. In other publications of ours, syphilis has already been pointed out as one of the causes of morphinism, of cocainism, and, in its ultimate result, of crime. This is not the place to study other arguments, since we must confine our attention to the consideration of pauperism. The man who suffers mental agonies on account of his face being deturpated with ugly sores, his limbs being painful and hard to move on account of syphilitic arthritis, has nothing else to which to turn but a public hospital.

The treatment and the better nutrition help the physical condition of the patient, but they do not improve him mentally. He gets better and is discharged from the hospital. He has already found out that he is dependent, and if unfortunately he has a family, their independence is undoubtedly destroyed. On the ground of sickness they apply for private alms or for public outdoor relief. Charity, although kind, especially if from a private source, has in its ultimate result the degradation of the family and, more particularly, the loss of self-respect. When the self-respect is lost the whole family may remain for their life nothing else than paupers.

The pauper, destitute not only of the necessities of life, but of his physical efficiency, depends on others for relief. The relief even then obtained for accidental occasions in temporary need, may sometimes cause the person to ask for a continuance of relief and to become addicted to seeking gratuitous maintenance. A pauper undergoes a mental

and physical degeneration, which causes him to become incapable of self-support.

In the present social condition, too, a man, suffering pains when released from the hospital, cannot easily find work. On account of his poor health, he cannot continue to earn his living for himself and for his family if he has one, and, as a consequence, when facing starvation, he may become a pauper or a criminal. According to R. L. Dugdale,[2] the choice would rest entirely on the temperament of the person, since more vigorous men and women become criminals, while the weaker ones become paupers.

The pauper, in many cases, is responsible himself for his misery and degradation, since in case of habitual inebriety or in newly contracted syphilis, he fails to be treated, and in this way loses his physical ability to work.

Syphilis is that disease which affects every organ of the body by causing destruction and impairment of its functions. After gonorrhea, syphilitic diseases of the eye are the most frequent cause of blindness. The eye is affected, in the secondary period, and in the tertiary period of the acquired disease, but in a great many cases children become blind on account of hereditary syphilis.

In the secondary period, the conjunctiva is often affected with syphilitic papules, or even gummatous infiltration, which maintain a reddened condition of the conjunctiva in the form of chronic conjunctivitis. In these cases, on account of the long standing process, a thickening of the conjunctiva may result in a form of pterygium. Affections of the cornea, according to the observations of Hutchinson, have been found quite frequent as a manifestation of syphilis, either acquired or from hereditary taint. The commonest form is that of keratitis parenchymatosa, which sometimes also is accompanied by troubles of the ear.

Syphilitic iritis is an affection quite common in lues, and we can say that more than one-half of the inflammatory affections of the iris are of syphilitic origin. Iritis is found in the secondary as well as in the tertiary period. Iritis is often associated with choroiditis and retinitis. In the earlier stages of syphilis it has a papular form, in the shape of pinhead nodules, which can be seen in the body of the iris or at the pupillary margin; in the later stage it is of a gummatous nature, appearing as a small yellowish-red nodule imbedded in the corner of the iris. As result of this affection, posterior synechiæ, or even occlusion of the pupil, may take place with necessary impairment of the vision. In some cases repeated inflammations of the iris and of the choroid may end with secondary glaucoma.

In affections of the intracranial portions of the optic nerve, or when gummata of the brain and its meninges are present, optic neuritis in its various forms may occur within the cranial cavity. From the syphilitic attacks on the blood-vessels, neuroretinitis may arise as was referred by Ostwald, Haab, Leggel, and H. Magnus. Amblyopia and amaurosis are the unfortunate consequences of cerebral syphilis.

We are indebted to Dr. Louis Stricker, of Cincinnati, a member of the Blind Relief Commission of Hamilton County, for the following report of his studies of the relation of syphilis to blindness:—

In my work as a member of the Blind Relief Commission of Hamilton County, I have examined up to date 417 applications for the pension, and in every case a critical study was made to ascertain the cause of the blindness and the disease from which the individual lost his sight. I herewith give you the figures:—

Total number examined			417		
Total number syphilitic			96	Of these congenital	41
				Acquired	55
Congenital.					
Malformations	Microphthalmus	2			
	Buphthalmus	1	3		
Phthisis Bulbi			2		
Interstitial Keratitis			1		
Uveal Disease	Irido-cyclitis	3			
	Uveitis	2	5		
Cataracts	Polar	1			
	Zonular	5			
	Luxated	1			
	Membranous	1			
	Soft	2	10		
Retina.	Choroidoretinitis	5			
	Retinitis Pigmentosa	3			
	Embolism C Artery	1	9		
Optic Nerve	Atrophy		11		
	Total		41	*Complications.*	
	Not on the Pension List		5	Mentally Defective	5
				Locomotor Ataxia	1
Acquired.					
General Uveal Disease			8		
Trigeminal involvement with secondary ulceration of the cornea. (Mooren Ulcer)			1		
Retinitis Pigmentosa			1		
Choroidoretinitis			8		
Optic Atrophy			37		
Total			55	*Complications.*	
Not on the Pension List			5	Insanity	1
				Locomotor Ataxia	17

On the Pension List.	Congenital	36 at 37.50	$5.400.00
	Acquired	50 at 37.50	7,500.00
Cost of Syphilis to the County, per Year			$12,900.00

From the report of Dr. Stricker it appears, that the number of unfortunates who have lost their eyesight in consequence of syphilis, acquired or hereditary, is 25 per cent. The cost to the county to provide in some

way for those dependents is $12,900.00 per year. Yet almost in every city the blind are permitted to beg, as there is no adequate public provision for their support.

This clearly shows that syphilis, by depriving a person of his vision faculty, is a cause of pauperism. Syphilis, however, affects every organ and every tissue of the body, especially the nervous system, producing the most varied forms of neuroses and psychoses. It exerts a great influence in the production of idiots and of feebleminded, who are often left to the care of relatives.

Nosography.—The man, who had that little chancre some five, ten or more years ago, which had been nearly forgotten, is suffering with rheumatism. He goes to bed at night to rest from the hard toiling of the day, pains affect his head in the form of neuralgia, or his legs as *dolores osteocopi, dolores nocturni.* He cannot sleep, cannot get one hour's rest. At dawn he must get up and go to work. The poor man is willing to work, to support his family, but has little efficiency, has no strength after passing sleepless nights, cannot earn what is necessary for himself and family, and soon understands that he is afflicted with sickness and poverty. He and his family deprived of the necessities of life must apply to dispensaries for medicines, for treatment, and then apply for relief, which although temporary is continued for a long time and may place that family among paupers. Charitable organizations state that about one-fourth of distress is caused by sickness, and nearly half of this fourth, in the opinion of the writer, is to be assigned to syphilis.

Syphilis is the cause of incurable gangrenous ulcers of the legs, and of other parts of the body. It causes obstinate arthritis of different joints. The incurable and crippled who are helpless are numerous in large communities and in general are not sufficiently taken care of in the cities. When syphilis has been neglected in the beginning, then considered ordinarily a mild case, it takes hold of the whole organism, and appears late in life in the most varied forms of chronic osteochondritis or of periosteal gummata. In the form of arthritis it produces effusions in the joints—hydrarthrosis, and as osteochondritis,—subluxation, pseudarthrosis, and immobility of the affected joints.

Those cripples and those affected with incurable ulcers of the legs are usually beggars. They are paupers, confirmed paupers. They beg and the little they obtain, they spend for alcoholic drinks. They sleep in lodging-houses, and when they have not the dime for a bed they apply to the station-house. The ulcers are left to themselves, vermin take hold of the whole bodies of those unfortunates, and then they are taken to the hospital. They are assigned to the dermatological service. Their clothes are alive with lice, their ulcers are covered with maggots. In this condition they come to our ward. Half stupid, trembling, they are scarcely able to reply to the questions. Usually they are old customers, known for many years to us and to our nurses. Bichloride is the grandest remedy to kill

bugs and clean the dirty surface of the ulcers. With the abstinence from liquors, with good food, some rest, external and internal specific treatment, the ulcers heal up, the arthritis improves, the patients take on a better appearance, and they are discharged. Soon after they leave the hospital they return to the saloon, begin to drink again, then occasionally go for thirty days to the workhouse, return to the same miserable condition, apply again to the hospital, again come to the dermatological service. Finally to get rid of them we send them to the County Infirmary. In these cases, without doubt, the reason of pauperism rests entirely upon the individual. If the individual, however, would have been healthy and had retained his efficiency he would never have reduced himself to such an abominable condition, and would have worked. These are other cases where syphilis is responsible for their poverty and for their depravation.

Apoplexy and paralysis in a man above sixty years is in most cases the result of syphilis, which is so deleterious in its action on the blood-vessels. When a man is paralytic, the welfare of the whole family, when depending on him, is gone. It stops his earning power entirely. In some cases, of course, the oldest children can provide for the family. Sometimes the wife, too, has been slightly infected and her health becomes delicate. Often she suffers with cephalagia, has leg ulcers, which make her unfit for wage-earning.

From the same syphilitic origin pitiable cases occur, which are not the offspring of our imagination, but are facts of our experience. The mother has given birth to a tainted child, the babe is sick, keeps fretting, is sleepless, can hardly breathe on account of snuffles, is covered with a papular eruption, and has mucous patches of the mouth. The poor creature is suffering for the sins of its father. It is not always so clearly indicated that syphilis affects the tainted babe, since there are some forms of disease, which although not exactly syphilitic manifestations, are nevertheless the results of a hereditary luetic taint. In a great many cases laryngismus stridulus, eclampsia, infantile paralysis, chorea, and even epilepsia are produced not by special hypothetical bacilli, but by the spirochæta pallida given to the offspring at the time of generation by the parents. In this case let us consider what happens in the family. The father may be sufficiently well able to work, but at night instead of resting, he is compelled to help the mother to nurse the child. In the morning he is tired, and unfit to take up another day's hard work; as a result he may lose his position, the whole family remaining destitute, without means of support. Here is the terrible association of sickness with poverty.

It is not only a few families that suffer sickness and poverty on account of this treacherous disease, but many are compelled to apply for relief on account of inability to work brought on by syphilis. The latest attacks of syphilis on the nervous system in the form of paralysis, of general paresis, or of locomotor ataxia, are quite frequent and make the man

unfit for work. In those families every valuable thing is sold to keep up the expenses, and when there are no more means the patient is sent to the City or County Infirmary and is a pauper, a charge on the community. These forms of nervous affections have been grouped in a separate class as parasyphilitic diseases. The reason is that the antisyphilitic remedies have no beneficial influence on them; moreover, they are made worse by the use of mercurials and the iodides. But although they are called parasyphilitic, the Wassermann test has shown the positive reaction of the blood in most of these cases, conclusively proving that they are the sad end of syphilis on the delicate cells of the nervous structures.

In the Cleveland Asylum for the Insane were fourteen men and two women affected with insanity caused by syphilis. In the Athens Asylum for the Insane only one was insane from venereal disease, but twelve were affected with epilepsy. Many cases of insanity are ascribed to bodily diseases, hereditary influence, congenital defects. Syphilis is not mentioned. From the report of the Board of the State Charities of Ohio[3] it is found that in the different Asylums and Infirmaries of the State there were five hundred and forty-nine epileptics, six hundred and forty idiotic and one hundred and forty-one deformed. It is not difficult to see that epilepsy, idiocy and deformities are usually the work of syphilis due to hereditary or congenital transmission. This population of epileptics, idiotics, and deformed, constituted an element which was distributed in the different Institutions of the State, and was in custody as paupers. All these Infirmaries and Asylums entailed an expense for the State of $680,657.08.

It is astonishing that in all the reports of the State Institutions[4] syphilis is not mentioned. We looked over the report of Athens State Hospital, Ohio School for the Blind, Toledo State Hospital, Ohio State School for the Deaf, Ohio Institution for Feebleminded, Ohio Hospital for Epileptics, Girls Industrial Home, Masillon State Reformatory, and many others, and syphilis, as a cause of these defects, could not be found mentioned even once.

In the Hamilton County Infirmary, where we have sent incurable patients with ulcerated gummata and osteochondritis, no diagnosis of syphilis can be found.

Yet we are more than satisfied that syphilis is at the bottom of most of those ailments, which cause the pauperism for which charitable institutions are crowded. Charity Organization Societies[5] refer to drunkenness and sickness as the principal causes of pauperism and as responsible for the distress of 35 to 50 per cent. of all applicants for charity.

Syphilis is contracted every year by a large percentage of people, and it is well known that 75 per cent. of all cases of syphilis are brought on, on account of indiscretion, but in 25 per cent. the disease is taken accidentally, as Bulkley[6] and others have clearly shown.

To have an idea of how many are infected with syphilis we are using

the statistics collected by Dr. S. Pollitzer and given in the transactions of the American Dermatological Association. These reports, however, are very deficient, because they give account only of eleven or twelve cities, and then solely of such cases as came under the observation of the members of that Association. They appear under the head of syphiloderma:—

1900. . .	2129
1901. . .	2995
1902. . .	2129
1903. . .	2744
1904. . .	2613
1905. . .	3153
1906. . .	2847
1907. . .	3644
1908. . .	3644
1909. . .	3661
Total	29,359

This means that in the last ten years the number of infected patients treated by the members of the American Dermatological Association amounted to 29,359 syphilitic patients in eleven cities: Boston, Buffalo, Chicago, Cincinnati, Cleveland, New York, New Orleans, Philadelphia, Washington, St. Louis and Montreal. This, however, represents only a fraction, when we think how many syphilitic patients are treated by their family physician, by advertising quacks, by druggists, by themselves, or are sent to Hot Springs. Moreover, every year it appears under the diagnosis of *ulcus* in over 500 cases, and as *ulcus molle* in over 400 cases. It is well known that *ulcus induratum* is the first manifestation of the syphilitic infection. It is the place where the inoculation of the syphilitic virus has taken place, and where the serum containing the spirochæta pallida has found its entrance. There is the place where the incubation is effected, and the spirillum of syphilis, which seems to be a form of protozoön, is developing and multiplying. It is the nest from which in forty or sixty days, millions of spirochætæ will start in the circulation in the lymph-vessels in the interstices of the tissues, to invade every organ and every tissue of the system.

Ulcus molle is positively non-syphilitic; it is only a local venereal ulcer, highly contagious, which after it has healed up does not leave any permanent trouble. But a great many times ulcers look like chancroids, are called chancroids, yet after twenty days tending towards cicatrization, the scar is somewhat hard, the lymph-glands are swollen and hard. This shows that it was a case of mixed chancre, which means that the diagnosis *ulcus molle* was accounted to one case of a true syphilitic initial lesion. In some of these cases the chancre is scarcely noticeable, so much so that the patients say that they had never had a chancre. But they say they had the bubo, as the gland nearest to the chancre gets hard and swells, and so remains for a long time without suppurating. In this case the

place of elaboration of the virus has been in the glands, and from there it has spread to the system. In some cases the gland may also suppurate, the suppuration is greater around the lymph-glands as peri-adenitis and the glands are really infected. These limited, incomplete statistics can only give a faint idea of the number of people who are infected with lues. Our interest in the matter will be greatly increased when we think that every one of these infected people must take treatment for three, four and more years. This entails a large expense to the individuals for treatment, and quite often loss of work, and loss of time resulting in further material financial loss. So far we have covered only those cases in which the individual can take care of himself, but when poor young men, who are living on their earnings day by day, are disabled, they must seek shelter in a hospital for treatment. In a great many instances the doors of the hospitals are found closed, and these poor fellows are turned into the street (dire irony), by those religious people who are preaching charity and asking contributions for charitable institutions. We have already dwelled on this subject in this JOURNAL, Vol. XVII., No. 3, 1910, when we pleaded for some interstate rules for the treatment of venereal diseases as a means of diminishing their diffusion. When thought is given to the fact that each individual is a possible active centre of contagion, we can realize what an appalling menace this disease not only may become, but actually is.

Any rule of any character which can stop the evil has to be accepted as the cheapest and the most humane. Ignorance, filth, disease, and poverty are the combined foes of civilization, and they lead unfortunately to pauperism.

Morphinism and cocainism in many instances are among the consequences of syphilis. The man who is troubled at night with pains—*dolores vaghi, dolores osteocopi chephalea nocturna*—and wants to have sleep, seeks relief, and his ultimate resort is to take morphia, or cocaine. This relieves him, he finds himself happy to have the means of relieving his pain, and of obtaining some sleep. One of our best physicians, who died a few years ago in performing a surgical operation, was accidentally infected with syphilis. The initial lesion began under the nail of the third finger of his right hand. When he came for an examination, his body was covered thickly with syphilitic roseola. He treated himself with only potassium iodide at different intervals. A short time after, he began to complain of *la grippe*. All his pains due to the deleterious action of syphilis, he attributed to *la grippe*. Whiskey and morphia were the remedies he chose so as to diminish these sufferings. The hospital was the only place where he could be cared for.

From our experience of many years in the hospitals we can state that syphilis is more prevalent in the lower classes of society. Syphilis combined with poverty makes a heavy burden, and to bear both of them it is excessive and unnecessary. Poverty and sickness form a terrible part-

nership, which add misery to the poor. The man afflicted with syphilis is at another disadvantage, he must bear his sufferings in silence, trying to conceal his sickness. He tries his best to continue his work, knowing that if he stops work misery will result.

Cause.—To the spreading of syphilis contributes a great deal the idea of vagrancy. The vagrant in winter remains in the large centres of population, moves from one lodging house to another, and in summer he goes to the country. These nomadic vagrants frequent special districts of the cities, which are usually patronized by the rough elements, called *town bums.* In these districts vice flourishes, as for example in the Tenderloin district in New York, South Clark street in Chicago, red-light district in Cincinnati, etc. There are small hotels, gambling houses, houses for the sporty elements of different grades according to the class of people who patronize the places. In these districts are found single men and single women, who have no matrimonial ties or disregard them. The men patronize saloons and lodging houses, and the women crowd dance halls and brothels. Young men from the country seeking work, poor clerks who seek a place where they can live cheaply, emigrants trying to find employment, come in contact with these elements, and naturally they get vicious, and in many cases acquire venereal diseases, adding sickness to poverty.

The vagrant class is usually recruited from the unemployed, they have no ambition for work, are usually suffering from ravages of venereal diseases, or from chronic ailments which are the result of syphilis. They form a class of indigent and infirm. They cannot, nor do they want to find employment; they are usually dependent and are not capable of being restored to usefulness and independence. Their life passes from the saloons in the slums, to the workhouse, from the workhouse to the hospital, then finally to the City Infirmary. This miserable condition is entirely due to vice, which has made them its victims, either by accident or by evil home environment.

Overcrowding is the cause of great evil. It has been demonstrated that pauperism, immorality, perverted sensuality, drunkenness and debauchery are in many instances caused by overcrowded tenements. Debauchery is in many cases the cause of syphilis, which, as a contagious disease, is found more abundantly in overcrowded districts. In the tenement houses there is to be found promiscuous mixing of different ages and sexes in a single room, which removes the sense of modesty and brings about corruption of the young people.

Prevention.—An approximate estimate of the cost to the community of the diseases caused by vice is hardly possible, but it is certain that it is a heavy burden. In the same way, the sufferings and the financial losses caused by these diseases to working people cannot be definitely calculated.

It is, therefore, a dire necessity to establish preventive measures to avoid syphilis, and society has the power to adopt them. This would

require the combined efforts of parents, of society, of clergymen, of physicians, of teachers and of the municipal authorities. The combined work may one day be rewarded with satisfactory results in the prevention of inebriety and in the prevention of syphilis and venereal diseases. The necessity of prevention and of special treatment has been so well felt and so well commenced against tuberculosis, that we sincerely hope that the same interest will be taken for the prevention of the hidden scourge of society.

It is a matter of incalculable importance for society in general and for the community in particular to preserve the productive forces instead of losing them. Prevention, and prompt treatment of syphilis can save great sufferings and heavy expenses. It is much cheaper to treat syphilis promptly and thoroughly than to leave infected people uncared for, and thus wait until the affection becomes a permanent infirmity with the consequent disability.

Preventive measures for diseases are indeed economical. These we would formulate in four paragraphs as follows:—

(1) Instruction and education, increase the standard of morality and inculcate high respect for the women.

(2) Diminish the overcrowding in the tenement houses. In factories and establishments where girls and boys are employed, rules of strict respect for each other must be enforced.

(3) Those who have been infected with syphilis must be treated. Hospitals have to take care of venereal patients, and dispensaries have to be within easy reach of everybody.

(4) Prostitution must be under municipal surveillance, and infected prostitutes must not be allowed to remain at large, but must be confined in hospitals and kept under treatment until the manifestations of lues are no longer dangerous for transmission.

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THE SANITARY SUPERVISION OF PROSTITUTES.*

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The Sanitary Supervision of Prostitutes, as provided for in Clause 79 of the Page Bill, has a most important interest to the members of this Society. The specific object of this Society's organization is to limit the spread of diseases growing out of the social evil. As stated in Article II. of its Constitution, it proposes to study every means, educational, sanitary, moral and administrative, which promises to be most effective for this purpose. It is eminently fitting, therefore, that we should study the preventive value, probable or presumptive, of this measure. If it promises to be effective in limiting the spread of venereal diseases, it should receive the endorsement and support of this Society. If, on the other hand, it should appear, upon examination, that it possesses no real efficacy as a preventive measure, and, moreover, has certain countervailing disadvantages which are calculated to work harm rather than good, this Society should endeavor to secure its modification or repeal.

While the purpose of this law is to a certain degree corrective and punitive, its essential intent as I understand it, is sanitary, and I shall consider it chiefly from this point of view.

Before examining in detail the practical working of this sanitary scheme, it may be well to survey the character of this legislation from a more general standpoint.

In the first place, it marks a new departure; in all previous legislation in this State dealing with the social evil, the diseases it engenders have been considered a negligible quantity and entirely ignored. This bill has the merit of recognizing the existence of these diseases, their significance as a danger to health, and the necessity of instituting measures to suppress them. The important question to be determined is whether the policy proposed represents advanced or retrogressive legislation.

As most of you are aware, opposition to this measure has developed in certain quarters, owing to the impression that the medical inspection of prostitutes is intended as an opening wedge to the State regulation of the social evil. This inference was, perhaps, legitimate in view of the fact that the statute is almost identical with that of the Continental System of

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Reglementation applying to the arrest of professional prostitutes and the medical examination of these women who, if found diseased, are remanded to the hospital for treatment until cured. Under the French law, amended April 11th, 1908, these provisions do not apply to girls under eighteen years of age. If they are arrested by mistake, they are immediately discharged, even if found diseased. While the measure under consideration is free from the odious feature of license, its administration carries with it the disgrace of a public trial, finger print impressions, etc., which are peculiar to our system of judicial procedure. It is more oppressive in that it permits a longer sentence to the hospital.

There is no suggestion that this legislation is reformatory in its purpose. Certainly no one familiar with the demoralizing influences and associations of a female venereal ward could be persuaded that they conduce to reformation of the woman or her restoration to a respectable, decent life. No prostitute was ever reformed by punishment. Its only effect is to render her more callous and confirm her in her nefarious calling. And yet, the class of women who chiefly fall under the provisions of this act are more likely to be the debutantes in vice, who are more susceptible to reforming influences. All medical experience is to the effect that the younger the woman the more apt she is to be found diseased.

This legislation is not intended in the interests of the diseased women themselves, unless we ascribe to the State an exaggerated paternalism which would supply skilled examiners and prolonged support and hospital treatment at the public expense, the economic cost of which would be considerable. Evidently it is in the interests of the men these women might infect.

The most distinctive character of this bill then is that of class legislation; speaking broadly, it is based upon sex. It is directed against a particular class of women for the protection of a particular class of men. Not the good citizens who lead regular lives, and to whom the prostitute with her cortege of infections carries no menace, but for the protection of the licentious class of men who seek these women for immoral purposes. Nothing could be farther from my idea than to intimate that the excellent men who are responsible for this legislation had any such purpose in view, but we are considering the practical operation of this law, and not the motives of those who framed it. It is to be borne in mind that venereal diseases are differentiated from all other infectious diseases by the peculiarity that they are commonly contracted through the voluntary act of the individual. Venereal disease seeks no man, it must be sought for in order to be acquired; with the exception of accidental and innocent infections it can only be acquired through an act which is qualified as immoral: it may easily be avoided by refraining from that act. Now the important question arises whether the State is under obligations to protect men from disease who are amply able to protect themselves simply by avoiding exposure to probable or certain sources of contagion. The State

cannot consistently make safe provisions for the gratification of man's sensual impulses without recognizing the doctrine that sexual debauch is a necessity for men.

Sweeping aside these conditions, the advocates of this measure may say: Let us be practical; prostitution has always existed; it always will exist; let us accept the situation as we find it. Men will consort with prostitutes, why not afford what measure of protection we can. Common sense would indicate that if these diseased women are returned to the streets they will infallibly infect a certain number of men. If they are isolated in the hospitals and cured, this given number of men will escape.

This conclusion by no means follows. It is infinitely more probable that these men with immoral tendencies will seek other prostitutes and be contaminated just the same; the supply of infectious material is always amply sufficient.

"But at least you will admit," they say, "that if one hundred or five hundred diseased women are sent to the hospital and cured, the number of active foci of contagion will be numerically reduced by just so many." Unfortunately the sum does not work out that way; it involves addition as well as subtraction. If a certain number of the inmates of disorderly houses are withdrawn, the revenue of these houses is correspondingly diminished. Commercial instinct would prompt the keepers of these houses to apply to procurers, to white slavers, and to other agencies for a new supply of women to take their places. These new recruits are speedily infected and the number of active foci of contagion is augmented rather than diminished. The supply of these women is always created to satisfy the demand. Such is the history of this vile commerce the world over.

Coming now to the practical workings of this sanitary scheme: In the administration of this law the police agent furnishes the testimony which convicts the woman of prostitution, and the physician furnishes the evidence necessary to convict her of disease. The consignment of the woman to the hospital is dependent upon the verdict of the examining physician, and her discharge from the hospital upon the certificate of the attending physician that she is cured. The physician acts as the judicial officer, the magistrate having no authority in the matter.

Medical Examination.—Now, the law, in requiring a *prompt* report from the examining physician as to whether or not a prostitute is diseased demands what medical science and skill are utterly unable to furnish. While it may be comparatively easy to recognize the presence of acute gonorrhea, these women, for obvious reasons, seldom practice their vocation with the disease in this stage; the vast majority of infections originate from chronic or latent gonorrhea. When the disease is localized in the deeper organs, the clinical evidence and bacteriological proof of its existence are exceedingly difficult or impossible to establish, and yet the disease may be actively contagious. The testimony of all specialists is concurrent upon this point,—that in these cases it is impossible to de-

termine with certainty the presence or absence of contagious elements. Neisser, the discoverer of the gonococcus, examined five hundred and seventy-two public women of Breslau. By the ordinary examination he found a discharge suspicious of gonorrhea in only twenty-two. By a more careful and thorough examination, he found that two hundred and sixteen of these women were indubitably gonorrheic or probably so. In fifty-seven of the others the contagious elements were not demonstrated but were regarded as suspicious. Professor Ehlers, for many years physician to the police, (*Bureau de Moeurs*) in Copenhagen, declares that a negative certificate has no positive value.

Nothing is easier than the diagnosis of syphilis in the active stage of secondary eruption; but syphilis is not a disease of continuous symptoms. In the intervals between the outbreaks, when the disease is in the contagious stage, there may be absolutely no evidence of its existence, yet there may be an explosion of contagious elements a few days thereafter. Then again, it is often difficult to distinguish between the eruption of syphilis and that of many common skin diseases which it simulates. The Wassermann test to discover the presence or absence of syphilitic elements in the blood, while most valuable, cannot be absolutely relied upon. It may be negative when the disease is undoubtedly present; it is frequently positive long after the individual has ceased to be contagious, so that after all we must rely upon the clinical evidence.

Commitment to the Hospital.—One obstacle in the administration of this law which our legislators did not forsee is the lack of adequate provisions for the treatment of this class of patients in the public hospitals of this city. There is not a single hospital on Manhattan Island which receives and treats venereal patients, the city provides only 26 beds in the City Hospital for female venereal patients, and about the same number in the Metropolitan Hospital, both on Blackwell's Island; the King's County Hospital and the Long Island College Hospital have each about twenty-five beds for this class of patients. In the existing organization of our hospital system there is not accommodation for one in five hundred of the prostitutes in this city. As a result of these inadequate provisions, the diseased women who have thus far been sentenced to the hospital under this law, have been confined in the cells of the Workhouse, which it is needless to say, is in direct violation of the express provisions of the statute. In this connection I may state that I have repeatedly called attention to the shameful and notoriously inadequate facilities for the hospital treatment of venereal patients in this city. About the only good I see in this law is that it may compel the authorities to correct this abuse.

I understand that arrangements are now being made to accommodate a limited number of these women by opening up a ward of forty beds in the City Hospital. But this evidently will suffice for only a small percentage of diseased women who will be sentenced under this law, if it is

honestly enforced. A legal measure is, to say the least, ill-considered if it requires impossibilities of the public functionaries who are to administer it.

What will be the effect on the City Hospital so far as its future efficiency is concerned? We should not lose sight of the fact that the moment a hospital begins to serve as a house of correction or a penitentiary a stigma is placed upon it which repels other patients. You may not be aware that the City Hospital was formerly known as the "Penitentiary Hospital," to which venereal cases were committed by the courts for treatment. Other patients refused to go there. The name was changed to the "Island Hospital," then to the "Charity Hospital," but its sinister reputation clung to it. It was finally changed to the City Hospital. It required nearly two generations for it to live down its unsavory reputation. Why repeat this experience?

Cure.—Now as regards hospital treatment and cure, it may be said that in the light of our present positive knowledge of the prolonged contagious activity of syphilis for years, and that of chronic gonorrhea, which may persist indefinitely, the assignment of a time limit for the cure of these diseases is unwarranted. The contagious laws of these diseases do not lend themselves to legislative enactments. The treatment of chronic gonorrhea in women is the most difficult and prolonged in medical therapeutics. Many cases cannot be cured without the removal of the deeper organs in which the germs find lodgment. If a woman is cured, she may be reinfected an hour after she leaves the hospital. Syphilis cannot be cured in one year, two, or even three years, and in many cases the disease is contagious during a much longer period. These cases may be whitewashed—that is cleared up of existing manifestations, but they are not cured. Time and time again in my twenty years experience in the City Hospital I have discharged syphilitic women free from every manifestation of the disease. They have returned in a short time, it may be a week or a month later, in as bad a condition as before; alcohol and dissipation promptly determine a new explosion of contagious elements.

In appreciating the value of the medical examination and hospital treatment of these women, it is well to weigh the results of the observation and experience of skilled specialists abroad where this system has been in vogue for a long period. Janet, the recognized highest authority on gonorrhea in France, and an ardent advocate of regulation, declares that the attempt to eliminate cases of gonorrhea by medical inspection and treatment in the hospital is like pouring water through a sieve. He, therefore, urges that the medical examination and isolation of these women be applied only to syphilitic cases. According to this authority, all prostitutes have gonorrhea,—in most of whom it exists in a torpid state without inflammatory reaction. He says: "In my opinion, if you wish to lock them up for that, it is necessary to lock all of them up." Another authority thus phrases it: "Why examine prostitutes for gonorrhea. They

all have it; we know in advance that they do. It is no less useless to cure them, since they are destined to receive every day their dose of gonococci."

Admitting for the sake of argument that the enforcement of this law is in the interest of the public health, if the principle be sound, if it is to be adopted as a settled State policy, why stop at half-way measures, why limit its application to the comparatively few women apprehended by the present haphazard and capricious methods of police intervention? Why not extend its advantages to the inmates of disorderly houses and the great body of prostitutes in the city, who according to the best medical testimony are practically all diseased. If it be a good sanitary procedure, the more thorough its application, the greater the protection to the public health. Why not adopt the vastly more comprehensive system of medical inspection employed in continental countries, which involves weekly examinations of all prostitutes who can be brought under police control, with the view of promptly weeding out sources of contagion as soon as detected.

Owing to inherent defects failure has been largely writ upon this system to limit disease. It is defective in that the medical examination fails to detect disease, the detention in the hospital is insufficient for a cure, the syphilitic cases are simply whitewashed and the gonorrheal cases, if cured, are incessantly reinoculated. In countries where it has been most perfected and employed, it has been condemned by its practical results. Fournier, its most distinguished advocate, says: "It does a little good, but it does not diminish the sum total of venereal morbidity." It is proper to state that Fournier believes that the inmates of disorderly houses who are closely subjected to sanitary supervision furnish the "minimum of nocuity," so far as contagion is concerned. This may be explained on the ground that the majority of these women are the older, more seasoned prostitutes who have been infected with syphilis at an early period of their career, have passed the contagious stage, and therefore cannot communicate syphilis, while those affected by gonorrhea have been instructed in the use of antiseptic douches and other preventive measures, so that they are less liable to communicate their disease. All experience shows that the younger the prostitute the more dangerous she is as the source of contagion.

Dr. LePileur, for fifteen years chief of the St. Lazare Hospital, says: "We receive every year more than one thousand of these women; about five hundred are new cases; more than one-half are the *réentrants*. They are arrested and sent back some two or three or even ten times during the year for recurrences of their disease." So that there is a constant procession of these women from the streets to the hospital, back to the streets, and again to the hospital. Of interest in this connection is the fact that of 56,196 arrests of women by the *Police des Moeurs* in a single year in Paris, this number embraced only 5,776 different women,—averaging more than 9 arrests to each woman.

One incidental bad effect which is inseparable from the operation of this measure should be noted. In the estimation of the public not only every woman discharged from the hospital—but, also every woman who successfully runs the gauntlet of the medical examination,—is regarded as safe. The failure of the medical examiner to detect disease is accepted as a guarantee of a clean bill of health. By thus furnishing what may be an illusory sense of safety, it cannot fail to act as an incitation to debauch.

The advocates of this measure may, however, say: "Why not 'try out' this plan? Why condemn it in advance? It is yet only in the experimental stage." To this it may be replied that it has already been tried for over a century in European countries, and has been abolished in many of them. As a matter of fact, no other plan has ever been seriously tried.

The germ of this idea may be found in the prescription of a famous medical ecclesiastic soon after the irruption of syphilis into Europe at the close of the fifteenth century. "Over 400 years ago, Gaspard Torella, who was Bishop Saint Just (Sardinia) and physician to the famous Caesar Borgia, promised to suffering humanity the eradication of syphilis in the following words: 'The *Mal Francais* may be exterminated with the aid of Almighty God and the Sainted Mother, Virgin Mary, if the Pope, the Emperor, the Kings and all other Princes will delegate the *matrones* to search out this malady and examine the public women, who should be isolated if they are found diseased, in a place to be especially indicated by the Prince, to be there submitted to medical treatment.'" (Ehlers.)

Notwithstanding the advances made in sanitary science and its brilliant achievements in the conquest of other infectious diseases,—this sanitary scheme serves as the model of all subsequent methods of dealing with these diseases. In spite of the accumulated experience as to its defects, and its failure, we still cling to this puerile and at the same time superannuated policy. I say superannuated, because while there may have been some justification for this policy when the opinion was held by the medical profession—as it was up to fifty years ago—that the contagion of syphilis began and ended with the chancre and that chronic gonorrhea was not contagious,—in the light of our present positive knowledge of the prolonged contagious activity of both these diseases and their contagiousness after apparent cure, the continuation of this policy is absurd.

When this prescription was given, syphilis was comparatively circumscribed; since then, it has invaded all civilized countries and is now practically world-wide in its extension—and by what agency? Evidently the naïve ecclesiastical physician overlooked the male factor in the spread of disease—the men who have carried civilization into new countries, have carried with them this sinister gift which infects and decimates the natives.

Now it may be considered foreign to the consideration of this bill to introduce that *other factor* in this discussion, but there can be no just appreciation of the value of a sanitary measure for the control of infectious

disease which does not take cognizance of the factors in its spread. The fatal defect of every sanitary scheme to control venereal disease has been that the masculine spreader of contagion has been entirely ignored as mythical or practically non-existent; the woman has been regarded not only as the chief offender against morality but the responsible cause of disease; all repressive measures to stamp out the diseases of vice have been directed against the woman alone.

This brings us to a brief consideration of the relative responsibility of these two factors. It may be positively affirmed that the male factor is *par excellence* the disseminator of venereal disease. He is chiefly responsible for its social consequences; and it is scarcely necessary to say that the social dangers of these diseases, their injury to the family, their significance as a racial danger, far transcend their injury to the health and life of the individual. The prostitute is but the purveyor of the infection; she returns to one or several consumers the infection she has received from another consumer; her pathogenic activities are confined to the field of immorality; while in this field she is undoubtedly the more active spreader of contagion, she rarely invades the habitations of virtue. It is her partner who carries the poison home and distributes it to his wife and children. He is directly responsible for the vast mass of disease engendered in the family,—the invalid and mutilated women, the sterile households, the blind children and the physical and mental weaklings, the defectives, which make up the hereditary horrors of syphilis. That he does this most often through ignorance does not alter the consequences.

If we are to make a just partition of responsibility for the spread of venereal diseases, let us be honest and decent about it. To paraphrase a sentence of the illustrious syphilographer, Dr. Charles Mauriac: Men infect women, but they do not wish to be infected themselves; in order to indulge their pleasant vices safely, they demand sanitary guarantees of women, but they offer none themselves—they pose as victims, while evading any responsibility for contagion, in defiance of the most elementary equity—this is the whole situation in a nutshell.

I have dwelt upon the responsible role of the male factor in the spread of venereal disease because there can be no intelligent or comprehensive scheme of prophylaxis devised which is unilateral in its workings. No Sanitary Bureau, no Health Board could stultify itself in attempting to control any infectious disease by isolating the female factor, while allowing the male factor to scatter broadcast the seeds of disease unfettered by a shadow of control. It would be a satire upon sanitary science, a travesty upon sanitary methods, an anachronism in the present advanced stage of preventive medicine.

The advocates of this measure may say: "If diseased prostitutes were retired from circulation and isolated until the contagious elements are sterilized by treatment, men would not be infected and they would not carry the infection into the family." But the cause of the evil lies deeper;

it is rooted in the physiological fallacy of the sexual necessity for men, the belief—fortified by generations of heredity and training,—that a man has a natural, unassailable right to indulge his sensual impulse as he pleases, and that the general principles of morality do not apply to his sexual conduct.

The double standard of sanitation has its exact counterpart in the double standard of morality; both spring from the same sentiment, or rather, the former is the direct outgrowth of the latter. Human society may construct a conventional code of morals to conform with its sensual inclinations, but the morality taught by science is more rigorous: the laws of infectious disease cannot be traversed or set aside to conform to an arbitrary discrimination based upon sex. Science recognizes the absolute equality of men and women before infection, as a logical conclusion; there should be equality of the moral law for the two sexes, equality of responsibility for diseases growing out of a violation of that law, equality of sanitary measures for their repression. It may be said that this idea is utopian and utterly unrealizable, but, in my opinion, it is the only key to the successful solution of this problem of prevention.

In my opinion, the tide of immorality which sweeps the country will never be stayed, so long as we hold to the ethical heresy that one-half of humanity has imperious duties that are not binding on the other half. The pestilential wave that follows in its wake, carrying the wreckage of the health and lives of innocent women and children will never be checked, so long as we hold to the sanitary fallacy that repressive measures should be applied to only one factor in the spread of disease.

Finally, another aspect of this legislation may be referred to: I am informed that this law meets with the approval of the magistrates, as it enables them to deal more effectively with disorderly women. Simply imposing a fine or sending them to the Workhouse for thirty days, it is claimed, does no good,—the object is to make the life of these women as hard and difficult as possible. No one will deny that in the interests of public order and decency every open manifestation of vice should be rigorously suppressed. The enforcement of this law may drive these women into temporary seclusion,—they do not like to be registered as criminals or subjected to prolonged imprisonment,—but the volume of vice and disease is not thereby diminished; it is simply diverted into other channels. If this legislation is intended to enable the magistrate to impose a heavier sentence than is now permitted under the statute applying to "vagrancy," the obvious remedy is to change the statute and not to invoke the intervention of the Health Department for such purpose. The extraordinary power over the liberty of the individual vested in the Health Board was intended to be used solely in the interest of the public health; it cannot be legitimately exercised for punitive purposes,—neither is it the function of the public hospital to serve as a house of correction.

It is evident that the more effective this law may prove as a police

measure the more defective it must be as a sanitary measure. Harsh punitive measures when applied to the treatment of contagious diseases always defeat the object in view, which is to treat as many cases as possible and not to drive them into concealment.

In expressing my honest conviction that this measure is unwise in its conception, defective in method, and possesses no real efficacy in the protection of the public health, I am by no means an advocate of sanitary nihilism. But if the State is to make any attempt toward the repression of venereal disease, let it be intelligent, comprehensive, and impartial, based upon sound scientific principles and sane sanitary methods. Let it not resort to a unilateral measure which has been condemned by its practical results elsewhere and is foredoomed to failure.

In the Chairman's report of the Committee of Seven, appointed by the New York County Medical Society in 1901, I advocated placing venereal diseases on the same plane of sanitary control as other infectious diseases dangerous to the public health, the entering wedge to this control being the obligatory notification of these diseases, under specified conditions, with due regard to their shameful character in popular estimation. Difficulties would doubtless be encountered just as in the case of tuberculosis, but they could be dealt with as they arise. Opposition to this measure would be largely disarmed by the assurance that this information would be kept secret by the sanitary authorities.

This policy is advocated with a full recognition of the fact that the prevention of these diseases is not purely a sanitary problem, and that we cannot successfully cope with this great social scourge by sanitary measures alone. They must be reinforced and strengthened by influences and agencies which can more effectively intervene in the correction of the causes of prostitution. Many of these causes lie entirely without the sphere of sanitary control. All experience shows that no communicable disease which is spread in the relations of family and social life can be successfully controlled without the intelligent coöperation of the public.

First of all the antiseptic principles of publicity should be applied to these diseases, the public should be enlightened as to their extent and their dangers,—both to the individual and to society,—and the laws of their contagion. Publicity of these evils is the first requisite; the public must recognize their existence and understand their significance in order to create a public opinion which shall sanction and sustain all measures adjudged necessary by the sanitary authorities for their effective control. I believe that the coöperation of the public waits upon this enlightenment.

The educational campaign inaugurated by this Society has not been confined to enlightenment of the public; it has been chiefly directed to the far more fundamental and radically effective work of educating the rising generation in the laws and hygiene of sex; to substituting sound, scientific, and wholesome knowledge for the sex instruction that the majority of young people pick up from ignorant and often vicious sources;

to the creation of a right mental attitude toward sex and sex relations; to the correction of certain physiological fallacies which constitute the strongest subjective stimulants to sexual debauch; and to enlightening young men as to the dangers, physical and moral, which result from irregular living—dangers which may have upon their future wives and children all the consequences of crime.

66 West 40th Street.

THE SCAPHOID SCAPULA SYNDROME; ITS CONNECTION WITH SYPHILIS IN THE ASCENDANTS.

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My observations have shown the scaphoid scapula to have far-reaching significance in the problems of heredity; to have unmistakable clinical

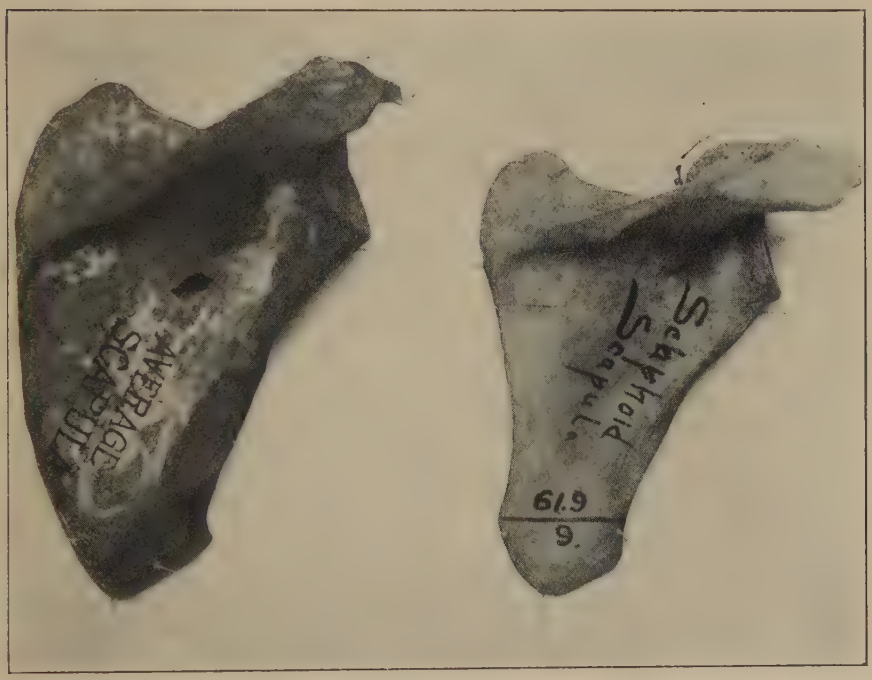

FIG. I.

significance and to be an anatomical entity. My studies of skeletal, embryo and monster scapulæ have shown that the scaphoid scapula, as a type, differs from the average scapula of the human race in several anatomical particulars, chief among which is that the vertebral border below the scapular spine is more or less concave—hence the name.* (Fig. 1.)

*The Scaphoid Scapula, a Frequent Anomaly in Development of Hereditary, Clinical and Anatomical Significance, *Medical Record*, May 21st, 1910.

Observing this type of scapula for the first time in September, 1906, in a seven-year-old epileptic boy, and later in his younger brother and sister, and in his mother, I have noted it many times since then, in the course of routine physical examinations. My observations warrant the prediction that studies by others will verify and establish the relative frequency of this anomaly in the population of cultured and civilized countries, and its very great frequency among backward and defective children, among epileptics, among the insane and among the so-called incorrigible and criminal classes.

Observing when the scaphoid scapula is found to a rather marked degree it is almost invariably associated with other anomalies, either physical or psychical or both, I have thought of it and now consider it merely one manifestation of some disturbing factor affecting the whole organism in its earliest development. I have found that it occurs in whole families, that it is transmitted from parent to child and so on through several generations, and that it is present in a varying degree in a large percentage of our population. The frequent occurrence of the scaphoid scapula in all branches of society seems to postulate a common cause and one sufficiently potent to modify the development of the growing organism from its very foundations.

From these observations and considerations and from my anatomical studies, I came early to the conclusions: (a) that no assumed circumstance in the life of the individual after his birth could give him the scaphoid scapula; (b) that its occurrence could only be accounted for by the assumption of some abnormal circumstance—some disturbing factor operating in the parents or in the more remote ascendants. Searching for the nature of the disturbing factor in certain individuals who have scaphoid scapulæ, I have found in them, in addition to disharmony in physical and mental development, definite physical signs, first and foremost of which is the presence of arterial changes, sclerotic changes, which we all recognize as keeping pace with advancing years after the fortieth year of life. But in certain individuals having scaphoid scapulæ, such changes appear much earlier than in average individuals, in some discernible by the ordinary methods of clinical investigation as early as the fourth and as a rule as early as the tenth year of life and in older individuals to a degree out of all proportion to their years. In such individuals I have also found with great frequency an abnormal degree of lymph gland palpability and the histories of catarrhal affections developing in early childhood and persisting for many years. During the earlier periods of life, many of these individuals have adenoids, not a few develop simple enlargement of the thyroid gland and some of them have nocturnal incontinence. Most of these clinical signs and conditions, as well as some others which I have learned to consider correlations of the scaphoid scapula, have been considered at some length in a recent article.*

*The Clinical Recognition of the Scaphoid Type of Scapula and of Some of its Correlations.

Aside from the chief correlation of the scaphoid type of scapula, namely, the deviating characteristics of the whole individual, the most constant, and, to my mind, the next in importance in certain of these is the presence of arteriosclerosis at unusually early periods of life, and in older individuals to a degree out of all proportion to their years. It was my recognition of early vasculosclerotic changes in certain individuals having scaphoid scapulæ which ultimately led me to the determination of one disturbing factor underlying the origin of this anomaly. Of the various causes, any one of which may so operate as to engender arterial changes in the individual, alcoholic and metallic poisons are considered pre-eminent. So far as I know, no one of these causes alone so affects the individual as to bring about even a tendency to arterial degenerations in his offspring. Furthermore, the conditions with which the scaphoid scapula is frequently found to be associated and its occurrence in all branches of society readily exclude any one of these factors as being the underlying cause.

There is but one disease known to me which permeates all branches of society; which may be transmitted from parent to child; which causes vasculosclerotic changes in the affected individual, as well as in his progeny, and that disease is syphilis. Syphilis is preëminently a vascular disease. Its pathology centers about its vascular manifestations. Whether the spirochæta pallida so affects the vessels in the growing embryo as to bring about disharmony in development, of which the scaphoid scapula may be only one manifestation, or whether this and other manifestations may be the result of its toxic products upon the germ plasm, I do not know. But that there is a strong connection between the occurrence of the scaphoid scapula in the offspring and syphilis in the parents or in the more remote ascendants, I have in my studies been able to demonstrate beyond all question.

Permit me to direct your attention to some known but not always appreciated facts which from the accumulated study of syphilis may be considered established, and to some personal observations bearing upon this connection. Of the very great number of our population who contract syphilis, only a few suffer from syphilis of the nervous system, tabes and general paresis. Nevertheless, syphilis of the nervous system, tabes and general paresis are believed by many observers to be becoming more frequent in our population, the latter making up an increasing percentage of the inmates of our hospitals for the insane. It is a matter of common observation that those who suffer from syphilis of the nervous system, tabes and general paresis are, as a rule, free from decided evidence of a former luetic infection as pertaining to the bones, skin and mucous surfaces. But that they frequently show a degree of vasculosclerotic changes beyond their years is not sufficiently recognized.

It is a matter of common observation that the malignant forms of syphilis, particularly as affecting the skin, bones and mucous surfaces are becoming yearly less frequent. My personal observations indicate that the

decided surface manifestations, as well as the malignant forms of acquired syphilis, are relatively infrequent in individuals having scaphoid scapulæ, and that in individuals suffering from tabes, general paresis, and syphilis of the nervous system, scaphoid scapulæ are frequently found.

May not the infrequency of malignant syphilis indicate that our population is acquiring a relative immunity from such forms because of the general syphilization of the race? May it not be that the gain in the infrequency of the surface manifestations of syphilis is more than balanced by the increased frequency of its later forms as affecting the deeper structures of the body and especially the nervous system? May not the presence of the scaphoid scapula in individuals suffering from the later and deeper manifestations of syphilis be an indication of its origin as well as of the individual's acquired relative immunity transmitted to him either from his parents or through them from his more remote ancestors?

Such observations, however, could never establish the origin of the scaphoid scapula, but they do seem to justify an inference of a strong connection between the occurrence of the scaphoid scapula in the offspring and syphilis in the ascendants. Now if this inference be well founded, we should find proof of it in our studies of the offspring of syphilitic parents; and we should expect to find proof not only in the study of such individuals as show the heretofore recognized signs of congenital syphilis, but in those we have heretofore considered free from every sign of hereditary "taint."

Our studies must not only apply to the individuals known to be of syphilitic parentage, but they must also apply to individuals coming before us in whom what may hereafter be called the scaphoid scapula syndrome is found. Not only must such individuals, their parents and more remote ascendants be studied from every angle, but the study must be made a comparative one. The individual presenting this syndrome must be compared with each member of his generation, with his parents, with his near relatives, when possible, with his more remote ancestors, and then the members of his generation must be compared, as far as possible, with other generations wherein syphilis has not existed in the parents.

Finally, all known facts in pathology bearing upon the recognition of congenital syphilis should be brought to bear in the study of individuals coming to section having scaphoid scapulæ, and especially upon the products of abortion. In such study there must be included the search for the spirochæta pallida and the determination of the vertebral borders in those embryos sufficiently advanced to permit of such a determination, and when possible, an attempt should be made to correlate the pathologic and bacteriologic findings with clinical data.

The heretofore recognized signs of congenital and so-called hereditary syphilis are relatively infrequent among the living children of syphilitic parentage. When these signs are absent, we have considered such children healthy or at least free from all effects of syphilis and we have

pointed to them as living examples of the triumphs of our therapy in the parents. Systematic and comparative studies of *all* individuals born of syphilitic parents will prove to anyone, who will take the time to make such studies, the fallacy of such conclusions. It is upon the evidence afforded by such studies that the final proof that syphilis is *one* etiological factor in the genetics of the scaphoid scapula must rest. Such studies on the part of many will, undoubtedly, broaden our conceptions concerning the evil effects of syphilis upon the offspring and at the same time determine the clinical worth of the scaphoid scapula syndrome.

Let us for the moment direct our attention to a composite picture of some of the physical and mental characteristics of individuals born of syphilitic parents and of their descendants and to some of the conditions and diseases to which my studies of such individuals have shown them to be peculiarly susceptible. Confining our studies in the beginning to individuals of the second generation, we shall find many of these to be of retrograding and deviating types. As a rule, these individuals will show, when studied in a comparative way, deviation in physical or mental characteristics and frequently in both.

Among such progeny with relative frequency will be found many of the heretofore recognized anatomic, physiologic, psychic and psychoneurotic stigmata and with great frequency the scaphoid scapula with its chief correlations in varying degrees. Such individuals are usually undersized, have sluggish attitudes, meagre musculature and are strikingly lacking in the harmonies of physical development. They range in stature from dwarfs to giants, but whether the one or the other or merely undersized, disharmony characterizes their physical development. Many of them, apparently physically normal at birth, in their later development show retardation, or grow by fits and starts until near, either before or after, the usual age of puberty when they shoot up like weeds or forever remain stunted—blighted.

With the beginning of mental development, such progeny are either backward and remain so, or they show, and this is the rule, precocity. If disharmony characterizes their physical development, it is especially true of their mental development. They seem to have no childhood and to jump from the cradle to adolescence. "My children are all old in their ways" is a frequent expression of certain observing mothers and they may add "They are almost always ailing;" or the unobserving mothers (ignorance, mother-love and pride makes them so) may proudly say "My children are all healthy." Indeed, physicians usually consider such children healthy or at least free from syphilitic *blight* in the absence of "snuffles," eruption of the skin and mucous surfaces, bone and joint affections, Hutchinson's teeth, interstitial keratitis and deafness without otitis. Children of the second generation are, as a rule, older than their years. They are often ailing and are rarely very healthy. To appreciate

the truth of these assertions, we must, as physicians, study the individuals of families as well as the histories of individuals of families.

While idiocy, imbecility and backwardness are found in the second generation, such mental states are by no means common. My studies of individuals of the second generation show precocious mental development to be the rule. Not only do such children appear like little old men and women in the seriousness of their ways and actions, their preference for books rather than play and for the society of their seniors rather than their kind; but, as individuals, their facial expression is lacking in the freshness of infancy, childhood and youth and they ever afterward appear much older than their years.

Many of them develop sexual instincts long before puberty and these instincts are often gratified by masturbation, sexual intercourse or otherwise. Strenuosity and intensity characterize many of these individuals and before or after adolescence such mental proclivities, associated with an inherently weak constitution, may sooner or later lead to a "break" and they make up a large percentage of the cases commonly classified as neurasthenia, hysteria and dementia præcox. Many cases of epilepsy, chorea minor and tic are to be found among individuals of the second and later generations, but especially in the second, and I have been greatly impressed by the unusual frequency of tuberculosis in these generations.

If the antenatal mortality of syphilitic progeny is so great, it is but reasonable to believe that the influences underlying it are still operative in the living. If not the disease itself, its blighting influence as manifested by disharmony in physical or mental development or both, by inability to stand the stress and strain of ordinary existence, by lowered general resistance and by degenerative and involutional changes. Such progeny are truly abiotic; hence the instability of their natures, their proneness to so-called functional nervous and psychical disturbance, to degenerative and involutional changes, to tuberculosis and other diseases. Not a few individuals of the second generation, despite their handicap in physical and mental endowments, learning to adjust themselves to their environment lead successful, useful, and even brilliant lives, though they rarely live out their expectancy in consequence of their abiotic natures.

In my first communication* I referred to vasculosclerotic changes as a sort of connecting thread between the syphilitic and his progeny. In my studies of many individuals and families, upon which this communication is based, a degree of such changes out of all proportion to their years is the one preëminent clinical fact discernible in individuals who have acquired syphilis and it is the one significant clinical fact discernible in their children and in their children's children. It is probably one cause of the frightful ante-natal and post-natal mortality among such progeny

*The Scaphoid Scapula, a Frequent Anomaly in Development of Hereditary, Clinical and Anatomical Significance, *Medical Record*, May 21st, 1910.

and probably the main cause of their abiotic natures leading to lessened expectancy in life and to their proneness to disease, to degenerative and involutional changes, to the so-called functional nervous and psychical disorders and the underlying cause of tuberculosis in them—for is not the blood the life thereof?

Since we have been able to trace vasculosclerotic changes as a sort of connecting thread between the syphilitic and his progeny, our ability to recognize such changes is of prime importance in establishing one cause of the scaphoid scapula. So constant are these, even by the ordinary methods of clinical investigation, that they will be rarely missed in syphilitics two or more years after infection or in their progeny after the tenth year of life. As an aid to the usual methods in detecting arteriosclerosis, permit me to call your attention to Luedde's modification of the Zapski Binocular Corneal Microscope with which we may readily see the blood coursing through the conjunctival vessels, and when present the thickening and aneurismal dilatations of their walls. The almost constancy of vasculosclerotic changes and our ability to recognize them so early in life in individuals of the second generation warrant the deduction that these changes begin during development in utero. In other words, that many of such individuals are born with a degree of arteriosclerosis. Such in brief have been the observations, the considerations and the manner of research which finally led me to the conclusion that syphilis is one cause of the scaphoid scapula syndrome and which enabled me to formulate certain laws (*Medical Record,* May 21st, 1910), which seem to govern the origin and transmission of the scaphoid scapula.

In conclusion, permit me to say that I consider my deductions by no means final. That there may be other causes than syphilis which may so operate as to affect the germ plasm of parents, the nutrition or the development of the embryo and thus bring about the scaphoid scapula, other disharmonies in development, early arterial changes and other correlations seems possible. I have searched for these in vain. If investigation by others should lead to the verification of my findings and deductions and thus establish the connection between the scaphoid scapula in the offspring and syphilis in the ascendants, even in a few instances, the presence of this anomaly may serve as a clue to more than one medical mystery.

Before we may determine the significance of the scaphoid scapula syndrome in any individual, he must be studied from every angle and in a comparative way with the members of his own family and with average members of the community. With the use of modern refinements in clinical investigation; with the use of laboratory methods, merely to confirm and to control clinical deductions; with patient study of individuals and of the individuals of families on the part of many workers, the cause or causes, as well as the hereditary, clinical and pathological significance of this syndrome, may readily be determined.

My studies thus far warrant me in saying at this time that such research on the part of many workers will undoubtedly lead to more complete recognition of syphilis and of its blighting influence in the individual affected, in his children, and in his children's children. Out of such recognition let us hope a sane prophylaxis may be developed, whereby much suffering which now comes to humanity from this insidious enemy of the human race may in succeeding generations pass away from the earth forever.

Metropolitan Building.

MEDICAL AND SURGICAL PROGRESS.

EHRLICH'S "606."

A REVIEW OF THE LITERATURE SINCE OCTOBER, 1910.

By Wm. Engelbach, M. D., of the Editorial Staff.

1. Alt: Die Behandlung der Syphilis mit dem Ehrlichschen Praeparat "606." (*Deut. med. Wochenschr.*, No. 41, p. 1889.)
2. Bardachzi and Klausner: Ehrlich's "606" in Syphilis. (*Wien. klin. Wochenschr.*, No. 44.)
3. Citron: Die Behandlung der Syphilis mit dem Ehrlichschen Praeparat "606." (*Deut. med. Wochenschr.*, No. 41, p. 1917.)
4. Dohi: Die Behandlung der Syphilis mit dem Ehrlichschen Praeparat "606." (*Deut. med. Wochenschr.*, No. 41, p. 1893.)
5. *Ehlers: Fatality After Injection of Ehrlich's "606." (*Muench. med. Wochenschr.*, No. 42.)
6. Ehrlich: Die Behandlung der Syphilis mit dem Ehrlichschen Praeparat "606." (*Deut. med. Wochenschr.*, No. 41, p. 1893.)
7. *Eitner: Blasenstoerungen und andere schwere Nebenerscheinungen nach einer Injektion von Ehrlich "606." (*Muench. med. Wochenschr.*, No. 45, p. 2345.)
8. Emery: The Preparation "606." (*Muench. med. Wochenschr.*, No. 45, p. 1543.)
9. *Fischer: Ehrlich's "606" in Syphilis. (*Med. Klinic*, No. 45.)
10. *Frenkel-Heiden: Die Anwendung des Ehrlich-Hata'schen Mittels bei Nervenkrankheiten. (*Berl. klin. Wochenschr.*, No. 45, p. 2048.)
11. Friedlaender: Die Behandlung der Syphilis mit dem Ehrlichschen Praeparat "606." (*Deut. med. Wochenschr.*, No. 41, p. 1915.)
12. *Gaucher: Sur la valeur comparée de l'arsenic organique et du mercure dans le traitement de la Syphilis. (*Bull. L'Acad. de Méd.*, November 15, p. 264.)
13. Glueck: Die Behandlung der Syphilis mit dem Ehrlichschen Praeparat "606." (*Deut. med. Wochenschr.*, No. 41, p. 1915.)
14. Gennerich: Erfahrungen ueber Applikationsart und Dosierung bei Ehrlich-Behandlung. (*Berl. klin. Wochenschr.*, No. 46, p. 2089.)
15. Grosz: (*Bull. L'Acad. de Méd.*, October 11, 1910, p. 180.)
16. Gruenfeld: Die Behandlung der Syphilis mit dem Ehrlichschen Praeparat "606." (*Deut. med. Wochenschr.*, No. 41, p. 1911.)
17. *Hallopeau: L'hectine ou le "606" dans le traitement abortif de la Syphilis. (*Bull. L'Acad. de Méd.*, October 4, 1910, p. 130.)

18. Iversen: Die Behandlung der Syphilis mit dem Ehrlichschen Praeparat "606." (*Deut. med. Wochenschr.*, No. 41, 1899.)
19. Lesser: Ehrlich's "606." (*Berl. klin. Wochenschr.*, No. 43.)
Marguelies: Die Behandlung der Syphilis mit dem Ehrlichschen Praeparat "606." (*Deut. med. Wochenschr.*, No. 41, p. 1907.)
20. Michaelis: *Ibid.*, p. 1912.
21. Miekley: *Ibid.*, p. 1903.
22. Nagelschmidt: *Ibid.*, p. 1922.
23. Neisser: *Ibid.*, p. 1889.
24. *Orth: *Ibid.*, p. 1903.
25. Pick: Die Behandlung der Syphilis mit dem Ehrlichschen Praeparat "606." (*Deut. med. Wochenschr.*, No. 41, p. 1924.)
*Ehrlich's "606" in Syphilis. (*Wiener klin. Wochenschr.*, No. 42.)
26. Polland and Knaur: Bericht ueber 50 mit Ehrlich-Hata "606" behandelte Luesfaelle. (*Wiener klin. Wochenschr.*, October 27th, 1910, p. 1521.)
27. *Riehl: Ueber Syphilisbehandlung mit Ehrlich's Heilmittel. (*Wiener klin. Wochenschr.*, No. 45, p. 1594.)
28. Rosenthal: Ueber "606." (*Berl. klin. Wochenschr.*, No. 47, p. 2137.)
29. Salmon: Die Behandlung der Syphilis mit dem Ehrlichschen Praeparat "606." (*Deut. med. Wochenschr.*, No. 41, p. 1918.)
30. Schanz: Das Ehrlichsche Praeparat "606" bei Augenkrankheiten. (*Muench. med. Wochenschr.*, No. 45, p. 2344.)
31. *Schindler: Die Behandlung der Syphilis mit dem Ehrlischen Praeparat "606." (*Deut. med. Wochenschr.*, No. 41, p. 1922.)
32. *Scholtz: *Ibid.*, p. 1910.
33. *Stern: *Ibid.*, p. 1908.
34. *Treupel: Weitere Erfahrungen mit Ehrlich-Hata Injektionen, insbesondere bei Lues des zentralen Nervensystems, bei Tabes und Paralyse. (*Muench. med. Wochenschr.*, No. 46, p. 2402.)
35. *Uhlenhuth: Die Behandlung der Syphilis mit dem Ehrlichschen Praeparat "606." (*Deut. med. Wochenschr.*, No. 41, p. 1906.)
36. *Umfrage ueber die Wirkung des Ehrlishchen Arsenobenzols bei Syphilis. (*Med. Klinik.*, No. 37.)
37. Volk and Lipschuetz: Die Behandlung der Syphilis mit dem Ehrlichschen "606." (*Deut. med. Wochenschr.*, No. 41, p. 1913.)
38. *Wechselmann: *Ibid.*, p. 1901.
Ueber oertliche und allgemeine Ueberempfindlichkeit bei der Anwendung von Dioxydiamido-arsenobenzol. (*Berlin klin. Wochenschr.*, No. 47, p. 2133.)
39. *Weintraud: Ehrlich's "606" in Syphilis. (*Med. Klin.*, No. 43.)
40. *Willige: Ueber Erfahrungen mit Ehrlich-Hata "606" an pyschiatrischneurologischen Material. (*Muench. med. Wochenschr.*, p. 2403, No. 46.)

A further study of the literature appearing on the subject of Ehrlich's new remedy, "606," since the last review [INTERSTATE MEDICAL JOURNAL for October], reveals a wealth of information issuing almost daily from investigators throughout the world. Perhaps no other discovery has created such universal interest as has been demonstrated by the in-

*The reviews marked with an asterisk contain the unfavorable results relating to the use of the drug.

numerable reports of the experimental research carried on with this "therapia sterilisans magna." The reason for this furor in medical circles is readily understood. A newly discovered drug, a single dose of which is lauded as a specific for one of the most general of infectious diseases, must necessarily be destined to receive such universal recognition. It is needless to say that the searching observations of so many investigators have developed many new phases which have an important bearing upon the use of this new remedy.

The earlier reports on the efficacy of "606" were so glowing that the action of this drug promised to be that of a harmless and magical specific. The reports communicated during the last two months demonstrate that there is a marked diversity of opinion, not present in the earlier writings, concerning the action and the application of this drug. Important problems appearing in these reports deal particularly with the specificity and toxicity of the remedy: the dosage, as to size, repetition, reaction and relation to conditions and different stages of the disease; newly undiscovered by-effects; technique of administration, such as menstruum and reaction of the preparation; and various methods of its introduction. The indications and counter-indications and the development of recurrences are important factors which have been given considerable investigation. The effect of "606" or a combination of arsenobenzol and other drugs upon other protozoal infections has also received some little attention.

It is not within the province of this review to attempt a solution of the many new problems which this therapy has introduced. For the sake of contrast, an analytical abstract of what are considered the most authoritative articles presenting both sides of this controversy has been essayed. Since this drug under the name of "Salvarsan" will soon be placed upon the market, the many conflicting reports concerning every phase of its usage should stimulate a continual, careful scrutiny of its actions and dangers as well as,—and this is more important,—discourage its indiscriminate exhibition.

The most noteworthy of the favorable communications was made before the Naturforscher Congress of German Scientists and Physicians at Koenigsberg. At this Congress Ehrlich, Neisser, Alt, Schreiber, Iversen, Wechselmann, Orth, and more than twenty-five other investigators, summarizing their personal experiences, discussed this new preparation from every point of view. Ehrlich recapitulated the more important facts deserving mention that have been made known since the introduction of his remedy, and added the more recent information that has appeared on that subject. He said the specific action of the remedy was recognized in animal experiments and was shown by the fact that on the application of a sufficient dose the spirochætæ disappear in twenty to forty-eight hours. If a longer time was required, either the dose was too small or the spirochætæ in question were immune to arsenic. The second fact which has developed was that specific antibodies are produced. Treatment with "606" furnishes an unusually favorable opportunity for the demonstration of these antibodies. The first important observation was that the milk of a mother, who was nursing a syphilitic child and was herself treated and cured with "606," had a most favorable action on the child. A similar result has been noticed in a large number of nursing women. The arsenic content of the milk is extraordinarily small, so that it was evident that the milk must contain antibodies which were received into the stomach of the child and absorbed. From other sources it is known that if the serum of such patients is injected into syphilitic children

the symptoms of the disease disappear. While it is evident that specific antibodies are formed, Ehrlich believes that the serum treatment alone is not sufficient for a positive cure, for, if of a thousand spirochætæ only a few survive, they are sufficient to prevent a complete cure. If children are injected with this serum, an immediate curative action is observed; the exanthemata very promptly disappear. But after six or seven days other disturbances develop, testifying that the antibodies are insufficient to destroy all the spirilla. It is, therefore, advisable to give such a child, soon after, a sufficient injection of "606" to kill the remaining spirochætæ.

The second specific action is the effect on the Wassermann reaction which is certainly concerned with the presence and growth of the spirilla. The very interesting observation has been made, that in certain affections a negative Wassermann reaction at first becomes positive under the influence of the injections. Thus, in chancres, at an early period, the number of spirochætæ is so small that they are not capable of producing a positive reaction. If the previously negative reaction is now at once converted into a positive one, evidence is furnished for the actual syphilitic nature of the disease. The importance of this reaction in the treatment with "606" cannot be sufficiently emphasized. If, in virtue of the therapeutic action, only 100 out of 1,000,000 spirochætæ survive, no reaction will occur, but every positive reaction is to be regarded as analogous to a relapse, and is, therefore, an indication for the repetition of the treatment with "606." Such cases should be examined at sufficient intervals and kept under observation. It would be very desirable if a modification of the Wassermann reaction could be made, so that the practitioner could apply this important test to his patients.

A third action which is very difficult to explain is that the remedy often works with wonderful rapidity. The statement has been made from many sources that patients, who for months had not been able to swallow any solid food on account of disease of the fauces or tonsils, could swallow immediately after an injection. This remarkable rapidity of action is not to be explained by anatomic changes, but depends on the removal of the pain, which was due to the action of the products of the secretion of the spirochætæ; "606" acts in this case as an analgesic. On the other hand, it has been occasionally observed that increased sensitiveness occurs in some patients similar to that observed after mercurial injections. The first observations in this respect came from Italy, where extraordinary caution was used and doses of 0.025 to 0.05 gm. (½ to 1 grain) were employed. The spirochætæ recovered themselves after a short time; they were not destroyed but were stimulated by the weak remedy so that the result was a great secretion of toxin.

Ehrlich has always regarded the drug as an arsenical and a dangerous remedy and has, therefore, insisted on the necessity of its thorough preliminary test. No one can expect absolute harmlessness in a remedy which is used to kill parasites. The mortality, following the use of the remedy, depends exclusively on the constitution of the patient, a law which holds for all dangerous remedies, even for chloroform. Ehrlich reported the use of "606" in 10,000 cases. The results demonstrated that "606" is not especially dangerous. In this large number of cases there was only one in which death immediately followed the administration of the remedy, and this was the case of a female patient whose disease, tertiary syphilis, must have eventually resulted fatally. In this case the injection was made with the acid solution and there was a certain shock which can be avoided with the

newer preparation. All other fatalities, of which the number might reach a dozen, occurred in cases of severe nervous disease,—tabes and the like,—in which the prognosis was very doubtful. If in such desperate cases unfavorable results ensue, it must not be concluded that the remedy is dangerous. Such extremely dangerous experiments must only be undertaken, if the physician has the conviction that he can save the patients, even though the patient could not be expected to become a useful member of society. A second contra-indication is furnished in diseases of the heart and blood-vessels in which the greatest caution must be observed. As to the technique, the alkaline solution which was first introduced by Alt and Iversen, has the slight disadvantage of being somewhat painful, while the neutral injection has the advantage of less pain. For that reason, the neutral emulsion should be preferred in neurasthenic and alcoholic persons and in patients sensitive to pain. Probably a combination of both methods, intravenous and subcutaneous injections, may be adopted. The dose depends upon the nature of the disease. A general dosage cannot be given. In nervous affections 0.4 gm. (6 grains) should not be exceeded, for these hypersensitive individuals react very unpleasantly in respect to the heart and central nervous system. Moreover, in these central nervous affections the number of spirochætæ is very small and a smaller amount of the remedy is probably sufficient for their destruction. It has been established that from 16 to 20 per cent. of the paralytics have lost their Wassermann reaction. These patients have not regained the reaction in a period of two years and this fact gives a most hopeful outlook for the future. In general, Ehrlich agrees with Neisser that the dose should be sufficiently large to effect a cure in one injection. In a relatively healthy person a dose as high as 0.8 to 1.0 gm. (12 to 15 grains) or even higher can be given without danger. Finally Ehrlich observes that the remedy is active in other diseases. Among these the most prominent are frambesia, which is very closely related to syphilis, chicken cholera, and certain forms of malaria. The fact has been independently established from various sources that a single subcutaneous dose was sufficient to relieve the fever in malaria. And in two smallpox cases, the remedy had an apparently favorable effect.

Neisser stated that the destructive action of the drug on the spirochætæ not only shortens the treatment of syphilis, but aids in restricting the spread of syphilis by promptly reducing the danger of contagion from the infected; although, he added, reinfections may probably be observed more frequently. He advises the combination of the tried method of treating the infection, although presumably it will not be necessary to keep up the old technique of seven or eight courses in the three or five years after infection. The serological test may reveal those who do not need continued treatment, but this is not always reliable, as experience has shown that after numerous negative responses the reaction may become positive and the symptoms may recur. Expectant waiting in these cases would lose the ground already won. The question now is whether the continued treatment, if deemed necessary, should be intermittent or continuous. The system may become accustomed to the drug and the spirochætæ may become drug-proof, while, on the other hand, with continuous treatment the special properties of the drug may display their best action. Early and energetic treatment with "606" in every case of syphilis he regards as a duty and does not rely on a single injection, but repeats the 0.6 gm. dose after three or six weeks, sometimes interposing mercurial treatment.

According to Alt, 75 per cent. of the mishaps reported to date might have been avoided by more scrupulous heed of the directions as to doses, solution, and administration. He stated that the drug not only kills all the accessible, fully-developed spirochætæ, but it induces hyperemia, local leucocytosis and mild inflammatory reaction in the syphilitic tissues and accumulations. When this process occurs in an enclosed space, as in the skull, the changes may entail transient symptoms of irritation or even paralysis. With syphilitic and parasyphilitic brain affections, slight sensory and motor symptoms may occur, but they generally prove transient. When paresis is so well developed that the untrained eye can recognize it, the affection has progressed beyond relief from any drug, benefit can be anticipated only during the stage of lightning pains. Especially in incipient taboparalysis the prospects are good for the treatment with "606." Cerebral syphilis, is a very convincing and grateful field for the new drug, but large doses should be avoided and the patient should be treated with as much caution as an epileptic with impending status epilepticus. The early forms of tabes have been much benefited in his experience; some of his tabetic patients treated last February and March have been freed to date (September) from their former attacks of pains. The effect of mere suggestion would probably have worn off long before this. One of his patients with pronounced ataxia last March, took part in the recent parade of veterans. He warns that tabetics are often in the habit of taking sedatives of various kinds with which one must reckon or untoward complications may result which might erroneously be attributed to the "606."

Wechselmann denounced the statement recently made that the "606" is equivalent to two doses of calomel, and reported a case in which the former apparently completely cured malignant syphilis which had resisted for four years numerous calomel and other mercurial and arsenical courses. The ulcerations on the penis had healed over only once and for a few days during the entire four years. After three injections of the "606" in the course of four months (0.25 m. 0.45 and 0.45 gm.) every process has healed and the patient's earning capacity has been entirely restored. He excludes from the treatment persons with flabby, weak myocardium, such as is often encountered in tabetics. Fever and an eruption are liable to follow the injection of the new drug when the heart is weak from any cuase, although this reaction always subsided harmlessly in two or three days in his cases. No injury of the optic nerve from the new drug has been observed to date. Local necrosis has developed more frequently and proved extremely indolent. Some of the tissues are still capable of recuperating, so that active measures are contra-indicated in treatment. Ehrlich called attention to the local necrosis observed after injection of the remedy in the breast of fowls; certain tissues seem more susceptible. In conclusion, Wechselmann declared that the efficacy of the new drug has been proved by the experiences to date, while its dangers have proved less than had been anticipated at first.

Miekley observed transient arsenic melanosis in an infant with inherited syphilis, but otherwise had no ill results of consequence to relate from his 157 cases. Marguelies reported extensive research with the new drug, which has confirmed the fact that the principle of complete sterilization by a single large dose can be successfully applied in all the trypanosome affections studied. Further, the spirilla do not become accustomed to the drug, so that equally effectual action may be anticipated with fractional dosage in spirilla affections. The animals did not

show any increased sensitiveness to the drug under repeated doses. Gruenfeld obtained the best results from the "606" in tertiary and inherited syphilis and found it harmless. (He added that armed with this new remedy flying squadrons might be organized and sent throughout the country to combat syphilis as effectually as the flying squadrons now handle eye-diseases in Russia. Hitherto the tediousness of the treatment of syphilis has prevented the organization of flying syphilis squadrons.) Grouven reported infiltration and painfulness at the site of the first injection after a second injection elsewhere, demonstrating irregular absorption of the drug, but otherwise had no special by-effects even with four repetitions of the injections,—no signs of anaphylaxis or diminution of efficiency. He also reported the curative action on an infected rabbit obtained with the blood serum from a patient treated with "606." Glueck stated that he had observed no bad results in 417 cases, although he had injected doses up to 0.8 gm. in some cases. Friedlaender advocated an injection of the new drug in every case of chancre without waiting for a certain diagnosis. He advises the continuation of treatment with "606" only when new symptoms develop. Nagelschmidt reported extensive experiences with "606" in cases of incipient tabes and advocated his technique which has given excellent results. He gives first a very small dose; this is often followed by excerbation of symptoms. He waits for this reaction to subside entirely, sometimes for one or several weeks, before he repeats the same or a little larger dose. Continuing in this cautious way with suitable intervals he has given up to 1.5 or 2 gm. of "606." Pick commented on the varying intensity of the reaction in different persons; the hysteric, neurasthenic and those with lively reflex action displaying the severest reactions.

Iversen recounts the successes he obtained with "606" in the treatment of relapsing fever. An injection of 0.3 gm. freed the blood from the spirilla in five to ten hours; hourly examinations after the treatment showed the progressive disappearance of the organisms. With the destruction of the latter, the fever would quickly fall and all the symptoms would be greatly ameliorated. This successful treatment of the spirillosis induced Iversen to try "606" in other protozoal infections, particularly in malaria; and he and his co-worker, Tuschnisky, experimented with the latter disease at Sotschi and Batum near the Black Sea. They treated 60 cases; 27 tertian, 4 quartan, 27 æstivo-autumnal and 2 tertio-autumnal infections. The drug was given in doses of 0.45 to 0.8 gm. intravenously and subcutaneously before, during, and after the paroxysms. In the tertian type the best results were obtained; 70 per cent. of the cases were cured by an intravenous injection of 0.5 gm., the plasmodia disappearing completely in twelve to twenty-four hours. No further paroxysms took place, the splenic tumor rapidly decreased and the general condition soon returned to normal. In the chronic cases with extremely large spleens the time for observation was too short to judge of the effect produced on that organ. In the remaining 30 per cent. of tertian cases, the clinical symptoms were quickly relieved, but the plasmodia could be found in the blood for some time after the injection. Quartan injections were less favorably affected; in two cases the paroxysms were rendered less intense and the plasmodia were not eliminated; in the other 2 cases, the drug had no appreciable effect either clinically or hematologically. The results in the æstivo-autumnal form, too, denoted no specific action on the part of "606." For, although the clinical course was improved, the headache relieved and the appetite improved, the fever curve remained

unchanged and the parasite could be found in the blood. In 4 cases the drug (0.5 gm.) induced an excerbation of the disease, similar to Herxheimer's phenomenon in syphilis; the fever became higher and more irregular, the chills more severe and the blood-picture was remarkably changed in that, in addition to the pre-existing crescents, there suddenly developed a large number of ring forms. In two other cases which exhibited only the ring forms, these disappeared with a sudden fall of temperature, but in five days, the fever returned and the blood showed the presence of the crescent type of the organism. From these investigations Iversen concludes that while "606" does not specifically affect all forms of malaria, it does exert a marked action on the tertian and, to a less extent, on the quartan and æstivo-autumnal varieties. He suggests that a combination of "606" with quinine or methylene-blue might be effective in all parasitic infection. It is this product that Iversen's associates in Batum are attempting to perfect at the present time.

Schanz discusses the use of "606" in specific ocular affections and compares the action of the new arsenical with that of atoxyl. These observations on the latter drug were made in his own clinic and in the practice of Werther and Galewski. More than 100 cases of blindness resulting from the use of atoxyl were collected. From his personal experience, and from the investigations of Birsch-Hirschfeld and Koster, who studied 46 cases of blindness due to atoxyl, he learns that this drug has a very characteristic effect on the optic nerve. Unlike other atrophies, changes in the fundus are found only months after the onset of visual disturbances. In atoxyl poisoning, the field of vision was narrowed on the nasal side, whereas central vision remained quite acute. Color-blindness, usually one of the earliest symptoms of atrophy of the disc, was delayed for a long time. In other toxic conditions, the pupil soon failed to respond to light, whereas this was not observed with atoxyl. The pupillo-muscular bundle usually first affected in other toxic amblyopias, was only gradually changed by the arsenical. Since atoxyl does not influence the optic nerve in the manner of toxemias, it seems plausible to conclude that it would not be concerned in activating a pre-existing lesion of that nerve. Although "606" should have an action similar to that of atoxyl, it does not affect the optic nerve in the same manner as the syphilitic toxin, and consequently it could not be conceived as exerting a supplementary action to the syphilitic process. In atoxyl poisoning, the symptoms of amblyopia followed within several weeks to seven months. This leads Schanz to conclude that if "606" possessed a similar toxicity, the announcement would have been made long before this. He has not observed any instances among his own cases, nor found any in the literature, that showed ocular changes following the use of "606." It is his belief that "606" has no harmful effect on the optic atrophy of syphilis, but will arrest the process when used in the early stages of tabes.

Grosz, Chief of First Ophthalmological Clinic in Budapest, has successfully treated 14 cases of ocular affections due to syphilis: An ulcer of the cornea, 3 cases of iritis, 1 of iridokeratitis, 1 of scleritis, 2 chordoretinitis and 6 of keratitis. Accordingly, he draws the conclusion that syphilitic eye-affections should not be included among the contra-indications of "606."

Lesser states that this preparation exerts the same action as other arsenicals in syphilis as well as in other spirilloses, only in a much simpler manner. The general condition improves, the patients regain their appetite, and their pallor yields to the tint of comparative health. This

organotropic effect is also the main factor in its efficacy in syphilis, as it reinforces the natural defensive processes. He believes the direct destructive action of the new remedy on the spirochætæ in the body is not the principal factor in the cure of syphilis. The dosage should be selected with the aim of influencing the natural defensive processes and increasing the vitality of the cells without reference to any direct destructive action on the spirochætæ. It has been his impression from his observation that the symptoms and the transformation of the Wassermann reaction are not influenced more by the large than by moderate doses. If the reaction is still positive six or eight weeks after the first injection, it might be advisable to repeat the dose. A negative reaction seems to indicate at least a temporary inactivity on the part of the spirochætæ.

Riehl recommends the more recent method of Ehrlich's technique, a combination of the intravenous (0.3 to 0.5 gm.) and the intramuscular methods as the best for giving this preparation. He intends adopting the method of first producing a tolerance to arsenic by giving increasing doses by the mouth, as was advocated by him in the treatment of psoriasis and lichen ruber, in order to bring about a less likelihood of arsenic intoxications from this drug in syphilis. Kern reported upon 123 cases which were treated in Riehl's clinic, 78 of which received neutral emulsion (Michaelis), and 45 a slightly alkaline emulsion (Blaschko) with favorable results, but said that the time was too short upon which to base reliable opinion with regard to its ultimate cure. Of this number, there were two recurrences in patients having severe ulcerative syphilides. In the majority of the cases the Wassermann reaction became negative after four to five weeks.

Gennerich experimented extensively in order to perfect the technique of giving "606," considering very exhaustively and scientifically, the dosage, reaction, and other details of the methods of application. His conclusion from his rather extensive investigations is as follows: "The subcutaneous method of a weak alkaline emulsion, according to Blaschko and Wechselmann, when the preparation is produced absolutely sterile, should not produce any local infiltration. The dose must be varied according to the lesions and stage of the disease." The lasting effect of an intramuscular injection is not necessary as evidenced by the results obtained from an intravenous injection upon the other malignant processes. If this is indicated, it should be obtained by a subcutaneous injection given three or four weeks after the initial one. A dose of 0.5 to 0.8 gm. is sufficient in one in the second stage of the disease, in which mercurial treatment has not been successful. A second subcutaneous injection is necessary in cases in which the Wassermann reaction has not become negative after forty days. In all the severe cases, especially malignant syphilis, a double injection according to Alt is indicated, *i. e.*, 0.5 gm. intravenously followed in two days by 0.6 gm. subcutaneously.

Polland and Knaur report the outcome upon 50 cases treated with "606," in the Dermatological Clinic in Vienna. Their conclusions are as follows: Initial scleroses are cleaned in twenty-four hours; begin to cover with epithelium in forty-eight hours; and are free from infiltration in six days. The scar and pigmentation are present in some cases as long as eight to fourteen days. Specific lymph-adenitis does not disappear within three weeks. Macular eruptions depending upon their intensity disappear from twelve hours to four days. Papular eruptions require one to two days longer; discharging flat papules, present for three to four

months, are dried in three days. Elevations disappear in ten days, leaving pigment. Hypertrophic and drying papules, after being present from nine to eighteen months, disappear in three weeks. Mucous patches are usually rapidly healed in from twelve to twenty-four hours. Specific iritis was cured in from four to eight days. Ulcerative pustular syphilides in early stages are free from discharge in two to three days and completely healed in ten days. The healing of gumma depends upon the location and size. Small flat gummata of the skin have been observed to heal in eight days. Others have required three to four weeks. Gummata of the palate and pharynx healed from fourteen to twenty-one days. Large papules of the septum in the palate were scarred over and covered with epithelium in three to four weeks. They have treated cases in which eye and heart complications existed without noticeable ill effect upon these organic lesions. They did observe rapidity of pulse, palpitation and irregularity in cases having atheroma of the aorta, and caution against the use of this drug in this condition even though it be of specific etiology. They conclude from their observation that this preparation undoubtedly has an intensity of action upon primary and secondary lesions, especially upon malignant syphilis which resisted the effects of mercury, that is far superior to any other therapy. It should be used with great caution in diseases of the heart and the aorta. They saw that its effect on parasyphilitic lesions of the nervous system is very uncertain and will require further investigation.

Rosenthal concludes from his own experience and from the study of the literature on this subject, that this new remedy is undoubtedly superior to any other single or combination treatment for syphilis. He emphasizes the fact, however, that a freedom from specific symptoms does not indicate the cure of syphilis, and that these cases should be observed particularly for the effect of this drug upon the serum reaction. He places for its positive indications primary lesion, ulcerative process, particularly of the mucous membrane, and malignant syphilis, the frequent recurrences of which do not react to mercury. He says it is yet entirely too early to say whether it is an absolute cure in a majority of the cases, and advises the profession not to forget entirely the already well-established treatment of this disease, which has been so successful in certain forms of its manifestations.

Emery, former head clinical physician of Dermatology and Syphilis, Saint Louis Hospital (Paris), who gave the injection to cases reported by Gaucher, made an exhaustive study of "606" in Germany, gathering his observations principally from the clinics of Herxheimer, Lesser, Wechselmann, Michaelis, Tomasczewski, Blaschko, Sachs and Neisser. His paper is very comprehensive in its consideration of all the varied aspects of the new treatment. The various topics are considered in the following order: *Technique.*—Every patient who is to receive an injection must have been previously examined with the greatest care. The fundus oculi requires the most minute examination. The urine is analyzed and various other examinations made. The patient treated must be kept in bed during the first two or three days, and after that confined to his room from six to ten days. In preparing the solution the most exacting asepsis must be followed, as sterilization is impossible after the preparation of the drug. The chief methods are the following: *Herxheimer's Process.*—Average dose, 0.50 gm. The powder requires careful trituration in a mortar. A solution of ⅓ c.cm. of 20 per cent. caustic soda is added, during the trituration. Then 10 c.cm. of water are added in small

quantities. The injection is made immediately so as to prevent separation and precipitation. *Blaschko's Process.*—20 per cent. solution of caustic soda of 1.225 density to which .09 gm. per dgm. of prepared powder is added, viz., 0.36 c.cm. for a dose of 0.5 gm. of powder "606." This is triturated for a long time and then 46 c.cm. of hot boiled water is added. *Michaelis's Process.*—For a dose of 0.5 gm. of the drug 1 to 2 c.cm. of ethylic alcohol is used as a solvent. Solution made in a test tube. 20 c.cm. of distilled *hot* water is added to this solution, gradually with continual stirring. When it is well dissolved, 1 c.cm. of normal caustic soda solution (40 per 1000) per dgm. of prepared powder is added. To the liquid from 2 to 3 drops of phenolphthalein (1 to 200) is added until it becomes red. Acetic acid is then added to this solution until it takes on the color of yellow sulphur. At this moment, 2 or 3 drops of the alkaline solution (Normal Na OH) are added in order to neutralize the excess of acid. Stop the operation when the upper part of the liquid shows a pink halo. The location chosen for the injection varies according to the choice of the operator. The injection of the substance is made at two periods of time, in one or two applications according to the quantity of liquid to be injected (5 to 25 c.cm.) and to the capacity of the syringe. The local and general reactions are seldom important. Pain seldom requires the use of morphia. The local swelling is rather similar to the reaction following the use of the insoluble mercurials. The rise of temperature is usually very slight, and occurs in 1 out of 4 cases. Constipation is more frequent than diarrhea. *Laboratory Control.*—The spirochætæ were frequently seen to disappear at the end of twenty-four to thirty-six hours; they seldom endured after six or seven days. Regarding the reaction of Wassermann, it was found to become negative in intervals varying from three weeks to two months. In comparison with this, the mercurial medication, even though it does produce negative seroreactions, seldom accomplishes this until after a prolonged intermittent course of treatment maintained during three or four years. *Evolution of Lesions after Treatment.*—Primary Lesion: The action of "606" seemed to be particularly rapid in a case of sclerosis of the lip which healed in three or four days. Genital lesions were clearing up in two or three days and were healed at the end of five to ten days. The action on the original lesion proved to be less striking than the recovery in other lesions, and this is explained by the vascular thrombi in the chancre, which to some extent oppose themselves between the medicament and its contact with the spirochætæ. This same phenomenon may be noticed with mercurial medication, especially when soluble preparations are employed. One must not conclude from these partial and exceptional failures, or from the slow action of the "606" that its efficiency is to be doubted at this stage of the malady. Perhaps the best results may be obtained by combining the general treatment and "606" with the local treatment of the chancre by means of the galvano-cautery, or mercurial ointment. However, it is in these cases of combined treatment ("606" and Hg.) that Ehrlich absolutely forbids the use of any other arsenical such as atoxyl or hectine. Secondary Lesions: The simple mucous patches of the tonsils and of the soft palate, and the erosive syphilides are more resistent, especially when influenced by neighboring suppurations. In Lesser's practice cases of extreme vulvar syphilis were healed completely in eight to twelve days, without any other local treatment than simple cleansing baths. The lesions gradually begin to disappear, sometimes in twenty-four hours, at other times five to six days after the injection. This

extraordinary efficiency and rapidity of action on contagious lesions suggests the important part that this specific is destined to play in the prophylaxis of syphilis. The eruptive lesions also gave way very rapidly under the drastic influence of "606." The granular syphilides react more quickly than the papular forms, and still more so than the papulo-granular forms of lichenoids. The skin of patients suffering from secondary specific eruptions is affected in a peculiar manner as was first reported by Herxheimer. During the first few days following the injection, macular spots appear, or if a roseola is already present, the individual lesions will be more congested, take on a very pinkish color and are increased in volume, and will sometimes be surrounded by new eruptive macules. When papular syphilides of various kinds are present, the lesions will be encircled with a kind of areola or rosy halo which gives them an appearance of a sudden aggravation. This additional eruption disappears rapidly and with it there is a cure of the original lesion. Herxheimer does not consider these reactions frequent, or unfavorable signs for a cure. On the contrary, they are, according to his opinion, the forerunner of a rapid regression of the lesions. In regard to the malignant syphilides, Emery considers their treatment a veritable triumph; for it is in these affections that the curative action of "606" is most complete and rapid. In several instances there was marked and rapid improvement in deep and extensive, inveterate forms of palmar and plantar keratosis. Tertiary Lesions: In this stage the use of "606" is followed by the most brilliant results. The action of the drug is particularly startling, for all ulcero-gummatous formations. Among other instances, are mentioned an enormous gummatous ulcer on the leg, two large contiguous gummatous ulcers of the tongue, a gumma on the roof of the mouth, all of which showed great improvement. Moreover, there were recoveries in a very grave case of gummatous, ulcerative, pharyngeal and perilaryngeal syphilis, and a case of diffuse hypertrophic syphiloma of the nose and upper lip. The treatment of visceral syphilis at the present time is the least studied, but mention may be made of syphilitic icterus cured in less than a week, ulceration of the rectum, and a serious recurring syphilis of the stomach that were benefited by "606." In regard to ocular syphilis, the improvement in conjunctivitis, choroiditis, and iritis was indubitable, but the treatment was too recent definitely to appreciate the results. In spite of the contra-indications established by Ehrlich, a number of cases of syphilis of the central nervous system have undergone treatment and showed a certain degree of improvement. In particular there is one case of cerebral syphilis presenting a threatening aspect, the symptoms of which were soon reduced to a few attacks of headache. A woman afflicted long since with syphilis showed amongst other pre-ataxic lesions a commencement of papillary atrophy; after the injection of "606" she was considerably improved in respect to the acuity of vision. *Hereditary Syphilis.*—Several cases have been benefited by the use of "606" at a very early age, but on account of the dangers entailed, only the mother receives the injection and the child in a number of instances has shown marked improvement by taking the maternal milk. *Relapses.—Emery has not been able to verify any case of relapse*, but some observers have remarked on them. This may be explained by the fact that the spirochætæ are only parasites of the blood in a very transient manner and leaving it set up isolated lesions in different parts of the body. These are apt to become active again and to return to the virulent state after some considerable time. *Non-Success.*—Emery has not been informed of any in-

stance of failure, but witnessed one case where a man was attacked with ulcerative syphilis on the cranium and face, and the lesions showed no modification about ten days after administering the injection. It was thought that there was a kind of encystment of the substance as was evidenced by the persistency of the tumor at the site of injection. It is perhaps for this reason that the investigators have recently begun vigorously to massage the injected part for at least ten minutes after the injection. Ehrlich noted that in cases where a very tardy cure occured it seemed to be due to the previous administration of arsenical preparations. Emery draws the following conclusions: 1. That at the present, this treatment is contra-indicated in elderly men; for all non-syphilitic visceral lesions-renal, cardiac, hepatic, splenic, pulmonary, and vascular affections, such as advanced aneurysm of the aorta; and in patients who have not a normal condition of the fundus oculi. In patients who suffer from a severe syphilitic affection of the brain, such as recent hemiplegia, acute or sub-acute meningo-encephalitis, it is necessary to observe the utmost caution, and, awaiting more ample information, to intervene only in very grave or desparate cases when mercury has ceased to be efficacious. Constitutional weakness and cachectic condition are not always contra-indications. 2. Indication for this treatment: (a) All lesions which do not yield to mercury; (b) for relapses immediately following an apparent cure with mercury; (c) repeated relapses; (d) total mercurial idiosyncrasy; (e) malignant syphilis, with secondary, or tertiary syphilides deeply destructive or mutilating; (f) initial lesions combined with radical local treatment. 3. That in every other case one may, according to the circumstances and fitness dependent upon the infection, use either Ehrlich's method or the old mercurial methods. He thinks, as do a number of writers on syphilis, these two methods of treatment assist and supplement each other in a certain number of cases. A long comparative study of the two kinds of treatment, of their advantages, their inconvenience, and their efficiency, will allow one to determine within their limits the precise indications for one or for the other.

Michaelis considers the reaction of the preparation and the most important factor in the technique of its administration. The question of the most efficient manner of dissolving the drug has not been entirely solved. In its free state it is insoluble and requires an acid or alkaline menstruum for its solution. It is least soluble in a very dilute alkaline or neutral mixture and this is the reaction of the blood and tissues in which the drug circulates after injection. This, he believes, explains its low degree of toxicity, as compared with other arsenicals, which are more readily dissolved in the fluids of the body. For this reason, it is never found in concentrated solution of the blood and attains no higher concentration than one to one thousand parts, irrespective of the alkaline or neutral character of the suspension. In contradiction to this, the actual facts prove that an alkaline solution acts with greater rapidity than the neutral suspension, and this investigator can offer no explanation for the tardy action of the neutral preparation. It is unlikely that an alkaline solution retains the same degree of alkalinity after as before the injection. After the solution is distributed by means of the lymph and blood-stream, it probably assumes the character of a neutral suspension. Michaelis follows the method of Wechselmann, but prefers the infra-axillary to the infra-scapular region as the site of injection and injects a neutral suspension directly into the muscles. The advantages are the absence of pain when the patient lies in the dorsal position and the more lasting effect from the slow absorption of the arsenic. Several immediate recoveries are reported, *e. g.*,

in a specific angina the pain disappeared in twelve hours and in a case of gumma of the lip of a month's duration, the swelling began to disappear in six hours.

According to Volk and Lipschuetz, the administration of "606" is greatly simplified and enhanced by suspending the drug in liquid paraffine or preferably in sterile olive oil, and then injecting the mixture beneath the skin of the back. In their 62 cases, they obtained favorable results with the exception of one case which was followed by a recurrence. They advise the use of large doses in recurrences, gummata, ulcerative syphilides, sclerosis and adenitis.

Citron attributes the unfavorable results following the use of "606" to the administration of acid preparations. He uses a syringe by means of which a definite proportion of calcium carbonate is added to the drug, thereby insuring a neutral solution. The advantages of this method are the following: The entire mixture is formed in the syringe and consequently may be kept sterile with the greatest ease; the use of the bland calcium carbonate does not occasion the irritative phenomena, so frequently observed after the use of the more caustic alkalies; moreover, accurate trituration is unnecessary with this method, since an excess of calcium carbonate is followed by no ill results. Citron obtained excellent results by applying this technique in animal experimentation. In 10 cases of syphilis in man, it produced no local or constitutional symptoms and did not modify the specific action of the drug.

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Among the unfavorable reports, those read before the French Academy of Medicine by Gaucher and Hallopeau offered the most adverse criticisms. That these unfavorable reports do not emanate entirely from French investigators is shown by the review of Fischer, Buschke, assistant in the Virchow Hospital, Berlin, as well as the reports of many other German authorities.

The report of Gaucher represents the results of three months of research conducted by this investigator and his associates. The problem was considered from the viewpoint of chemistry, pathology, physiology and clinical observations. Gaucher was assisted by Desmoulière in the chemical investigation, Paris in the pathology, and Lucien Camus and Jean Camus in the physiology of "606." The special organs were examined by various pathologists of repute. Emery administered the drug in the clinical cases. The results of the investigations were observed and confirmed by representatives of various countries who assisted Gaucher in his work. In order to comply with the laws of France, which prohibit the use of drugs of unknown composition, the cases for treatment were carefully selected; only those were accepted who repeatedly requested to be treated and were willing to relieve the invstigator of all rsponsibility in the event any complications should follow the use of the medicament. The report includes the following topics. *Chemistry.*—The drug yields the characteristic reaction of phenolcompounds when treated with a solution of ferric chloride. It reduces oxyhemoglobin as is shown by the spectroscope. Albumin is precipitated by an acid or neutral and, to a less degree, by an alkaline solution of "606." This precipitation is assisted by the addition of sodium chloride. *Pathology.*—Eleven guinea-pigs were injected with "606" in doses ranging from .009 to .12 gm. per 100 gm. of body weight and succumbed in one to thirteen days. In those that died in twenty-four hours (dose .01 to .012 gm.) the organs were intensely congested and contained hemorrhagic foci. The liver was enlarged; the

blood-vessels engorged; the trabeculæ were compressed and the hepatic cells around the portal radicles were infiltrated with fat. The kidneys were congested, especially in the cortex; interstitial and intralobular hemorrhages and a small cortical infarct was observed. The spleen was greatly congested; the Malpighian corpuscles were hypertrophied and infiltrated; the large white cells were increased and filled with blood-pigment, and there was a small thrombus which was partially organized. The suprarenal glands showed medullary engorgement; the heart was cyanotic and filled with agonal clots; the myocardium was congested. The lungs presented basal congestion and subpleural lobular hemorrhages. The intestines were filled with diarrheal material. In the animals that died on the fourth day, similar changes were found. Those that lived nine to thirteen days were affected to a slighter degree, the liver and kidneys presenting less important lesions. The toxic dose for guinea-pigs is .08 gm. per kilogram of body weight. The phenomena observed at autopsy correspond to evidences of arsenic poisoning. *Physiology.*—A number of experiments were performed on dogs and the following observations were made: Therapeutic doses (.01-.02 gm. per kilogram) in alkaline solutions introduced into the veins or muscles only slightly affect the blood-pressure and pulse-rate. Increased doses caused a fall of blood-pressure and a profound modification of the cardiac rhythm, the pulse becoming depressed, rapid, and irregular. In addition there followed vomiting, hematuria, respiratory increase, asphyxiation, and death. The intravenous injection of a neutral solution induced fatal embolism in two instances. *The coronary arteries showed multiple emboli from an albuminous precipitate of* "606." The epithelial and endothelial structures were most affected in these animals. But the marked susceptibility of the nervous structures is clearly evidenced in animal experimentation. Two rabbits died after receiving a spinal injection of .0075 gm., their death being preceded by convulsions and coma. In three instances dogs succumbed to minimum doses (.0035 .0025 gm.) which were injected into the cerebrospinal fluid. As to the reaction, guinea-pigs were more affected by alkaline solutions, which is due to the fact that alkaline solutions are distributed more rapidly. Neutral solutions of the drug occasioned a lower rate of mortality. Some of the animals injected with acid solutions were living at the time of this writing. The latter solutions are partially precipitated and therefore, are less toxic. *Clinical Observations.*—Gaucher states that "606" does not surpass hectine in its curative properties; that it affects only certain manifestations and that recurrences and exacerbations of the syphilitic process are very frequent. Seven cases are considered in detail to substantiate the statement that "606" is not permanently curative. Lesions of the skin and mucous membrane are, under certain conditions, greatly improved, but this may be due to the cicatrizing and not to the specific action of the drug, since arsenic has long been recognized as a keratolplastic agent. Mucous lesions were sometimes healed in two to four days; others, however, resisted the drug for a longer period and in some instances, were entirely unaffected. Ulcerous patches, in particular, are benefited only slowly or resist "606" entirely. Papular patches are very resistant. Chancres often disappear in two or three days, but ten days or even a longer period were required for complete cicatrization. Gummata disappear no more rapidly than with mercurial treatment. Tertiary lesions of the mouth are known to have disappeared in ten days when mercury was used. An oral gumma endured twenty days after the use of "606." The latter remedy is valuable, however, in gummatous formations which have resisted mercury. In several instances, cutaneous

gummata were not improved by the use of "606," and a number of ulcerous syphilides of the mouth were intractable or improved only after a period of four weeks. It was found that dry cutaneous lesions were less frequently improved than ulcerative conditions. Roseola readily disappear but papular lesions are more resistant. Lesions on hairy parts and tuberculous syphilides were removed with difficulty. Papular tuberculous syphilis showed no improvement a month after the injection of "606." Frequently, mild secondary lesions reacted well to the latter drug, but not with greater readiness than to benzoate of mercury. Remarkable results were observed in certain tertiary conditions, but on several occasions, there was a loss in weight, which detratced from the state of recovery. In regard to failures, no improvement was observed in syphilitic leukoplakia buccalis, tabes, and general paresis. Syphilis of the osseous system was not treated by Gaucher. Neither did he apply the remedy in nephritis, but he saw one case benefited and another rendered worse by the use of "606." From these investigations Gaucher concludes that Ehrlich's remedy is not curative; it does not prevent recurrences, regardless of the fact that it causes them to disappear. It affects cutaneous and mucous lesions, especially of the superficial and, to a less extent, of the ulcerative type. Its action is rapid, but not permanent. In some cases "606" is beneficial when mercury has failed, but on numerous occasions, it has not been proven to posses that superiority. In visceral syphilis, it shows no efficiency and may actually be detrimental.

Hallopeau reports extensively on the value of hectine as an abortive of syphilis in comparing its action with "606," other arsenical preparations, and the ordinary syphilitic treatment. He reports in detail many other favorable results obtained by this remedy (hectine) and believes that it will abort syphilis if properly given in the incipiency of the disease. He also reports cases of "606" having recurrences which were apparently cured by hectine. He gives detailed accounts of cases of his own, some of his colleagues which were only slightly benefited by "606." According to him "606" does not fulfill the conditions of harmlessness and of constancy of effect which alone would justify the interest taken in it. There have been, he says, fourteen deaths from its use, two in Paris, besides cases of blindness. These criticisms, he says, should be circulated by the lay press. Objections to Hallopeau's attitude ensued in the Academy. Dr. Netter, *agrégé* professor at the Paris Medical College, in discussing this paper, expressed surprise at hearing Hallopeau's unfavorable comment. The case of death mentioned, he said, could not be considered as due to the drug; and as for the cases of blindness, Netter had heard of none. He believed that great credit is due a man of such high standing and great scientific probity as Professor Ehrlich.

Fischer states that Buschke, whom he is assisting, declares that his extensive experience with the new remedy in the dermatological department of the Rudolf Virchow Hospital at Berlin has convinced him that it should be reserved exclusively for patients resistant to mercury. He has also encountered a few patients refractory to "606," and prolonged observation is showing that even when the primary manifestations have subsided under its influence, general symptoms are liable to develop later. The lesions which disappear so rapidly under the "606," are the kinds which promptly subside under any other method of treatment, the indurated chancres being more slowly influenced. In one case the chancre was found only slightly diminished and swarming with spirochætæ two months after the injection of the usual dose of "606," while the patient

has been tormented with extremely frequent and severe colic pains never observed before, and which Buschke ascribes to the arsenic. He says that no one seems to appreciate how rapidly syphilides may subside under ordinary treatment. Clinicians are surprised by the rapidity of the action of the "606," but, if they will keep records of the cases in which mercury alone was used, they will frequently find that the syphilides disappear as rapidly or even more rapidly under mercury. In a recent case a much debilitated man had numerous syphilitic ulcerations over his body, especially on the legs, with papulous syphilides on the back. Under salves and baths the ulcerations all healed over in twelve days and then mercury was commenced, under the influence of which the papulous syphilides soon healed. The man gained six pounds in three weeks. The tonic effects of the care and food in the hospitals have often an amazingly favorable action on the general health without any drugs or mercurial treatment. But "606" has displayed great efficacy in the severe and extensive syphilis refractory to mercury. This seems to be the special field of the new drug, although it may fail even here, as in a case Fischer has previously reported. Syphilis of the central nervous system also seems, in certain cases, to be amenable to the new drug, but special caution is required as cases have been reported in which no benefit but actual harm has followed its use; even fatalities have been reported. On the other hand calomel renders good service in these cases, especially in the recent cases. Recurrences after "606" have been frequently reported, but the question is whether the recurrences are exceptionally mild or not. In four cases in Fischer's experience the recurrences were unusually early and intense; in one case, the symptoms suggested arsenic intoxication but they might have been explained by some incipient syphilitic cerebrospinal trouble; but other symptoms suggested hysteria and an epileptiform seizure, and weakness of the right leg further complicated matters in respect to the share of the "606" in the syndrome. No ethylic alcohol had been used in injecting the "606." Rille and Spiethoff, too, have reported epileptiform seizures after its injection. In five other cases in which "606" had been injected on account of skin lesions, recurrences were observed taking the form of serous iritis in four and of neurochorioretinitis in the other. He can mention a number of similar cases observed by others, the recurring manifestations developing in the eyes. There was no ocular predisposition in any of these five cases, ophthalmological examination before the injection of "606" having shown normal conditions. He thinks that the new remedy probably has a special affinity for nerve tissue, and although it does not directly injure the nerve, like atoxyl and arsacetine, yet it provides a place of lessened resistance and here the syphilitic virus preferably locates a syphilis *ex trauma*.

Orth reported experiences with local necrosis in the buttocks after injection of "606." In the first case death followed the 10th day after the injection, but the tissues were bacteriologically sterile and there was no suppuration. In the second case the patient died from cancer in the throat 6 weeks after the injection; the necrotic patch still showed the yellow field around a hemorrhagic centre characteristic of this necrosis.

Rille and Pinkus have recently reported three cases of jaundice following administration of "606." The local necrosis sometimes observed is evidently of purely chemical nature; it is exceptionally torpid, and operative removal of the necrotic tissue if practically impossible as the necrosis goes very deep, the chemical action extending far into the interstices in the tissues. The breast is a particularly unfavorable point

for the injection on this account; in one patient the necrosis in the breast extends down and into the ribs and there is danger of perforation of the pleura. Only a part of the arsenic seems to be taken up into the tissues; the rest is slowly, possibly intermittently eliminated, and these factors vary in different individuals, so that it is unusually difficult to determine the tolerated dose. Fully as good therapeutic results have been observed with small as with large doses. Alt and Hoffman have reported severe cardiac symptoms after the injection of the new drug, and Fischer reports another grave case of this kind.

Bardachzi and Klausner found an increased proportion of urobilin in the urine after injection "606" in a number of patients, but the most striking effect was a remarkable transient increase or decrease in the red blood-corpuscles which was regularly observed in the patients whose blood was examined. The number of reds showed fluctuations of 1,000,000 or more in the seven cases cited, running from 5,750,000 to 4,300,000 in one case in twenty-four hours and dropping from 4,800,000 to 3,800,000 in another case.

Weintraud concludes from his experience in 125 cases that syphilis is not definitely cured by a single injection of "606" and that no benefit can be expected from it in tabes. The syphilitic infection may injure a predisposed nervous system to such an extent that even the most thorough treatment may not prevent the development of locomotor ataxia. In a few of his patients, the new remedy failed to display any therapeutic action, and the Wassermann reaction persisted unmodified in many of the patients; in others, after a negative phase, it became positive again in a few weeks. The negative phase after a treatment with "606," therefore, does not indicate a complete cure any more than after mercurial treatment. Recurrence was observed in 14 out of 80 cases of recent and secondary syphilis. In only 37 out of 77 patients, did the Wsasermann reaction remain negative. In three cases the Wassermann reaction persisted unmodified, even after a second and third injection of "606." He thinks it improbable that permanent results will follow increased dosage. In his experience intravenous infusion of the drug which brings the whole organism under its influence more thoroughly, was not followed by permanency of cure any more than with the other techniques. It seems that the body reacts as promptly and extensively to a small as to large amount of the drug, and this reaction is the chief aim in the treatment of human beings, while in an animal the purpose is to kill all the organisms at one injection. Repetition of the doses may prove as effectual as with mercury. None of the symptoms in his twenty cases of tabes seemed to be influenced by "606," but it displayed great efficacy in patient refractory or intolerant to mercury and iodine. There is grave danger that physicians and the public will regard the problem of the cure of syphilis as too simple and as already solved. It must be reiterated that the cure in man is a far more complicated process than the cure of experimental syphilis.

Uhlenhuth discusses the results of arsenicals obtained in the treatment of the spirilloses. He contrasts the reaction of atoxyl and atoxyl-saurin, a combination of atoxyl and mercury, with the results obtained from the use of "606." He concludes that the latter remedy while affecting syphilis more rapidly than do other arsenicals, is incapable of sterilizing the entire organism and effecting a complete cure in such chronic diseases as lues and sleeping-sickness. This is possible in other spirilloses, however, in which the organism itself aids in producing immunity by the production of antibodies.

Ehlers injected the drug according to the technique of Wechselmann. The patient was a man of forty with paralytic dementia which had improved considerably under psychiatric treatment, so that he was able to walk, read and understand part of what he read. He had had two apoplectiform attacks previously, one two years and one five weeks before the injection. The injection was not followed by any local reaction but progressive symptoms on the part of the nervous system developed. The patient died on the fiftieth day of progressive cardiac weakness. No cause for the fatality could be discovered at autopsy, except the parenchymatous degeneration of the organs.

Pick states that since his first publication, recurrence of symptoms has been observed in some of the cases previously reported. He encountered 6 refractory patients among the 200 that were treated.

Eitner reports a case in which an injection of "606" was followed by retention of urine and constipation, with abolition of the reflexes, the clinical picture being identical with that of the two cases reported from Prague. He never uses ethylic alcohol, so that the disturbances cannot be explained in this way, which was the explanation accepted for the Prague cases. He used for the injection a mixture of what was left in two tubes of "606," the greater part of the contents of the vials having been used in another case respectively fourteen and three days previously. The tips of the tubes were fused to protect the remaining contents, and he thinks that the heat applied in the fusing must have modified the drug in some way to render it more toxic. Experiments on animals with the "606," after it had been heated, seemed to confirm this assumption of a toxic modification of the drug under the influence of heat.

In regard to the sequellæ of the use of "606," Klingmueller and Pinkus report a case of gangrene, three cases of local necrosis, two of abscesses, three of toxic erythema, one of detrusor paralysis, one of tenesmus, and a case in which pre-existing diabetes became aggravated and still persists to date.

According to Frenkel-Heiden the reports of the nervous affections, supposedly cured by the use of "606," are not deserving of grave consideration. He believes it more important, in judging the character of improvement in these diseases, to observe the quality of the pupillary reaction than the subjective symptoms, such as the tabetic pains, etc., which often disappear without the application of any drugs. He concedes that active lesions of the nervous system readily respond to the curative action of "606," but states that in parasyphilitic diseases, the drug must be administered in exceedingly large doses. The question arises, therefore, whether it is justifiable to subject a patient to the dangers of such quantities of the drug, or whether the same results may be obtained by exhibiting the remedy in repeated doses in smaller amounts. Frenkel-Heiden offers reports of cases treated by other investigators, many of which prove the curative properties of the new remedy. The objection raised against the use of "606" is that the nervous tissue in tabes and paralysis is incapable of restitution. Nevertheless, the drug should be used in these diseases since the actual degree of degeneration is not known, and there always remains the possibility of arresting its progress. The relief of the pains in tabes and the improvement of the paretic ocular muscles should not always be ascribed to a regeneration of nerve-tissue, but possibly follow the removal of gummatous pressure on the meninges. The progress of tabes, in his opinion, is due more to the progressive arteriosclerosis and to intercurrent infections than to direct degeneration of the nervous tissue.

In the reports of nervous diseases he draws attention to the lack of analysis of the cerebro-spinal fluid and believes that such examinations would more definitely decide the action of "606" upon lesions of the cord. His conclusions are that Ehrlich's remedy is not contra-indicated in paralysis and tabes; that its use is not attended with danger; that it exerts a favorable action upon tertiary lesions of the central nervous system, but has very little effect, either favorable or unfavorable, upon parasyphilitic affections.

Willige reports upon the observation of 24 cases of tabio-paralysis in 35 cases of nervous syphilis and concludes as follows: The action of Ehrlich's preparation upon metasyphilitic diseases of the nervous system is uncertain. Some results indicate the possibility of improvement by this treatment, and a prevention of remissions of the disease. The method of giving increased doses, repeated smaller doses, or combining this drug with other treatment has not been established up to the present time. The best results were obtained from the repeated small doses. Ameliorating influence upon the Wassermann reaction was not observed. It produced no untoward effect upon the lesions of the individual in any of their cases. Optic atrophy was not considered as a proper indication for its use, nor did it have any bad effects upon severe forms of diabetes, which were present in a number of their cases.

Treupel reports on the extensive observation of the action of this drug upon specific diseases of the nervous system, in particular, tabes and paralysis. Some of these cases have been previously reported, and he gives the course of the disease since his last communication. In 6 cases of lues of the central nervous system, 4 reacted very favorably in a comparatively short time, and have had no recurrences of symptoms indicating lesions since their recovery. In 21 cases of tabes and tabio-paralysis, he gives the following favorable report: For two to three days, the lancinating pains would frequently be increased. After this they would gradually ameliorate and the general condition would improve, as was evidenced by gain in weight and strength. The paratesias and sphincter functions of the bladder would improve and the taxia would decrease. This improvement would exist for months, but would not be permanent. No material effect upon the pupils or reflex was observed in clinical cases. Optic atrophy was not increased in any of the cases. The Wassermann reaction became negative in a very small per cent. of cases. In 10 cases of progressive paralysis, some of which were in their incipiency, there was apparent arrest of the disease with the exception that they had to be confined. There was no chance of improvement in the objective symptoms of this disease during the nine months of observation. He concludes from his observation that, in diseases having already a degenerative process of the nervous system, this therapy will have little influence with regard to relief. Whether it will be able to stop the progress of incipient cases, can only be determined by more extensive investigations.

Wechselmann's most recent report deals with the susceptibility of certain individuals to arsenobenzol. From his large number of cases (over 900), he was impressed by the many different degrees of local and general reactions which followed the injection of this remedy in different individuals. The well-known local reaction already described following subcutaneous and intramuscular injections induced him to investigate this point with considerable detail. He was surprised to find that nervous women, who undertook the treatment with considerable apprehension, had a less painful local reaction than phlegmatic males. He found that the irritative reaction of the tissues, which usually occurs on the second or

third day, was due to more or less edema, which later changed into a connective-tissue mass followed, in some cases, by a hard infiltration or cyst, disappearing in from two to four weeks. This was not due to infection or reaction of the tissue to the caustic. It was present to a variable extent in different individuals. In some cases the infiltration was the size of a fist, appeared within a day and was followed in a short time by a brown necrotic slough. In other cases this change would take place at the end of the second week. The ulcer produced by this slough, held in its wall, arsenobenzol, and has been proven by him, as well as by Orth, as not being due to infection. Undoubtedly the susceptibility of the patient plays an important role in the technique of giving this drug. If the preparation is properly introduced subcutaneously ir intramuscularly, these bad effects can be avoided. On the contrary, if a subcutaneous injection is given too deep into the fascia, secondary irritative effects of arsenic, with the following of necrosis, is liable to take place. In those lean individuals, where there is an absence of adipose tissue, it is difficult to give a subcutaneous injection, which might not produce serious local reaction. In giving subcutaneous injections it is, therefore, necessary to see that the needle moves freely in a considerable circle beneath the skin, in order that it is not in the lower layers of the skin or the underlying fascia. The location should be selected which contains the most fat free from glandular tissue. Insert two needles and inject one-half of the substance through each needle, while moving the point of the same under the skin, so as to distribute the drug over considerable surface. In giving the intramuscular injections of the back, he also uses this technique of giving a small amount through a needle placed in one direction, and then by changing the direction of the needle the substance is distributed over considerable tissue area. Among the general reactions, that he observed in individuals considered by him susceptible to arsenic, are the following: One case (general paresis) had fever and a hyperemic area at the point of injection on the first day. The second day there were fever, a general exanthema, and conjunctivitis. The pulse remained good and the general condition was otherwise unchanged. The urine was free from blood and albumin. This case cleared up rapidly. In his later observation, he observed these reactions in certain individuals. (1 per cent. of his cases.) The incubation was eight to ten days with the initial symptoms of hyperemic area around the point of injection. Small herpes which soon changed into pustules formed over this hyperemic area. Usually about this time there were a rise in temperature and a more or less generalized scarlatinal exanthema accompanied by conjunctivitis. The exanthema occurs first about the extremities and spreads to the rest of the body. In some cases, gastric symptoms, diarrhea with considerable thirst, coated tongue, and sometimes vomiting occurred. The patient felt very sick, but the pulse was not much increased. The urine was free from albumin and sugar. The duration of the temperature was usually three or four days. In some cases there was a rise of temperature on the eighth or tenth day without the cutaneous mucous membrane lesions. He compares this reaction as similar to the anaphylaxis reaction of serums. He said that up to the present time, while he had had no serious unfavorable reactions, that his experience had forced him to caution against the use of this drug, particularly in cardiac complications. Furthermore, that it was necessary to continue to watch the effect of this drug very carefully in order to establish with more certainty the indications and the contra-indications for its usage.

THE CEREBROSPINAL FLUID IN SYPHILIS AND IN PARA-SYPHILITIC DISEASES.

A REVIEW OF RECENT LITERATURE.

By S. STROUSE, M. D., of the Editorial Staff.

1. Nonne and Apelt: Ueber fractionirte Eiweissausfallen in der Spinalfluessigkeit von Gesunden, Luetikern, functionell—und organisch Nervenkranken, und ueber ihre Verwerthung zur Differentialdiagnose der Dementia Paralytica, Tabes Dorsalis, tertiaeren und abgelaufenen Syphilis. (*Arch. f. Psych.,* 1907-08, xliii, 433.)
2. Nonne: Clinical Diagnosis of the Syphilogenous Diseases of the Central Nervous System. (*Jour. Amer. Med. Assoc.,* 1909, liii., 289.)
3. Noguchi and Moore: The Butyric-Acid Test for Syphilis in the Diagnosis of Metasyphilitic and Other Nervous Disorders. (*Jour. Exper. Med.,* 1909, xi., 604.)
4. Noguchi: The Serum Diagnosis of Syphilis. (J. B. Lippincott Co., Philadelphia, 1910.)
5. Jones: Modern Progress in Our Knowledge of the Pathology of General Paralysis. (*Lancet,* 1909, ii., 209.)
6. Jones: The Proteid Content of the Cerebrospinal Fluid in General Paralysis. (*Rev. of Neurology and Psychiatry,* 1909, vii., 379.)
7. Jones: A Review of Our Present Knowledge Concerning the Sero-Diagnosis of General Paralysis. (*Amer. Jour. Insanity,* 1909, lxv., 653.)
8. Ross and Jones: On the Use of Certain New Chemical Tests in the Diagnosis of General Paralysis and Tabes. (*Brit. Med. Jour.,* 1909, i., liii.)
9. Meyer: Zur Untersuchung des Liquor Cerebro-spinalis. (*Neurol. Centralb.,* 1909, viii., 786, 2204.)
10. McCampbell and Rowland: Studies on the Clinical Diagnosis of General Paralysis of the Insane. (*Jour. Med. Research,* 1910, xxii., 169.)
11. Marinesco: Sur la Diagnostic de la Paralysie Générale et du Tabes par les nouvelles Methodes. (*C. R. Soc. Biol.,* 1909, lxvi., 648.)
12. Gay and Fitzgerald: The Serum Diagnosis of Syphilis. (*Bost. Med. and Surg. Jour.,* 1909, clxi., 432.)
13. Mott: The Pathology of Syphilis of the Nervous System in the Light of Modern Research. (*Brit. Med. Jour.,* 1909, i., 454.)
14. Stillman: A Report Upon the Value of Noguchi's Reaction on Spinal Fluids. (*Proc. N. Y. Path. Soc.,* 1909, n. s., ix., 1-2.)
15. Amsden: Report of Certain Lumbar Punctures at Bloomingdale Hospital. (*N. Y. Med. Jour.,* 1910, xci., 438.)

16. Apelt: Beiträge zur Frage der Berechtigung der Spinalen und Cerebralen Punktion. (*Berl. Klin. Wochenschr.*, 1910, xlvii., 1540.)

A great part of the light of modern research on the pathology of syphilis has been turned on the question of the relation existing between syphilitic infection and general paralysis and tabes dorsalis. Many of the former assumptions have been proved to be scientific facts by the wide application of the Wassermann reaction and by detailed studies on the spinal fluid. Most of the latter investigations have been directed to chemical and cytological diagnostic aids, and the results have been in most cases absolutely conclusive. The normal cerebrospinal fluid contains such a small amount of protein as not to be detected by ordinary methods, whereas in the parasyphilitic affections there is an appreciable increase easily determined. As the protein that is increased is serum globulin, all tests proposed to measure this increase are those applicable to the determination of globulin; and those most commonly used may be briefly described. Nonne modified the original Nissl method by his now well-known Phase I., which consists in mixing equal parts of spinal fluid and a saturated solution of ammonium sulphate, and allowing the mixture to stand three minutes. At the end of this time a positive reaction is shown by the tube assuming an opalescence or definite cloudiness. The interpretation of the end reaction with this method is at times confusing, and to obviate this difficulty Ross and Jones modified it by making a ring test similar to Heller's nitric acid test for albumin in the urine. They float one part of the spinal fluid on two parts of a saturated solution of ammonium sulphate and examine the ring formed at the junction of the two fluids. Noguchi, while studying the chemistry of the serum reaction in syphilis, devised a very simple test for increased globulin, the use of which has given excellent results in the hands of most workers. To one part (0.01 c.cm.) of spinal fluid are added five parts of a ten per cent. solution of butyric acid in physiological salt, the tube brought to a boil, and immediately one part of normal sodium hydrate added. The tube is again boiled, and either immediately or within two hours a definite fine or granular precipitate is seen in positive cases. This is to be differentiated from a slight cloudiness which normal fluids may give. Although all three of these tests are supposed to indicate the same thing, there seems to be a general agreement that the two last described are more delicate and offer less difficulty of interpretation than Nonne's Phase I.

Considerable attention is being paid to the total cell count and the differential count of pathological spinal fluids. Normally there are a few cells, averaging from two to eight per c.cm., practically all of the small mononuclear type; but in many diseased conditions of the meninges a considerable increase appears. Most workers consider a total count above ten as indicative of a pathological condition, and in general paralysis and tabes one usually finds a variable increase, almost always of the small mononuclears. The technique of counting has not been altered to any extent, and is simply executed by means of the ordinary red blood-cell counting pipette, whereas the differential is made from a centrifugalized specimen in exactly the same manner as is done with blood.

Properly to appreciate the value of increased globulin and lymphocytosis one must realize that with the exception of the Wassermann there is nothing in the spinal fluid absolutely pathognomonic of syphilis, and the true estimate of their worth can be obtained only by careful correlation

with clinical findings. For instance, both increased globulin and lymphocytosis are present in inflammatory conditions of the meninges like tuberculous meningitis, but the clinical history of the latter condition is not likely to be confused with the history of general paralysis, tabes, or cerebral syphilis. It has been shown that in approximately ninety per cent. of all cases of tabes and paresis both the lymphocytosis and the globulin reaction are positive, whereas in other conditions of the central nervous system clinically resembling these both reactions are negative. They have been thoroughly tested in the neuroses and psychoses with negative results, less absolutely in such conditions as multiple sclerosis, idiopathic epilepsy, pseudo-tabes alcoholica (Nonne), tumor cerebri; and the studies so far undertaken are sufficient to warrant the statement that the presence of either the globulin or the lymphocytosis or both is presumptive evidence against the presence of a pure psychosis of non-syphilitic origin and in favor of general paralysis or tabes. As far as the relative delicacy of the tests are concerned, practically all authors are in agreement that since both represent the same pathological process they are of approximately equal value. In other words, when there is an increased cell count, there is likely to be an increased globulin fraction and vice versa, but at times either one may be present without the other. No explanation is offered for this apparent discrepancy and the opportunity still remains for further study on this point. Although the figures for the incidence of a positive Wassermann in the cerebro-spinal fluid in tabes and general paralysis vary from 50 to 95 per cent., there is no divergence from the opinion that lymphocytosis and increased globulin are present far more frequently than is the Wassermann; and although not as absolutely pathognomonic as the latter, they are extremely valuable, especially in connection with a positive Wassermann reaction in the blood.

In the diagnosis of cerebrospinal syphilis the tests are again of great value, but they are powerless in the differential diagnosis between direct syphilitic involvement of the central nervous system and the parasyphilitic affections. The Wassermann reaction is given by about 90 per cent. of all cases of cerebrospinal syphilis, and lymphocytosis and increased globulin in practically all. The absence of the reactions in brain tumor and in other conditions likely to be confused with the protean manifestations of syphilis of the nervous system renders the tests of extreme diagnostic value.

To summarize this abstract it can be said that in addition to the application of the Wassermann reaction attention is being paid to increased globulin and increased cell counts. The presence of these two conditions can be easily ascertained in cerebrospinal syphilis as well as in parasyphilis. In addition to being of great value in diagnosis they have also shed light on the underlying pathology of general paralysis and tabes dorsalis.

SERUM DIAGNOSIS OF SYPHILIS.

A REVIEW OF RECENT LITERATURE.

By Carl Fisch, M. D., of the Editorial Staff.

1. Clough: .Clinical Experience with the Wassermann Reaction. (*Johns Hopkins Hospital Bull.* No. 228, March, 1910.)
2. Beiker: Wassermann's Reaction and Narkosis. (*Deutsche Med. Wochschr.*, No. 13, 1910.)
3. Bruck and Stern: About the Character of the Wassermann Reaction in Syphilis. (*Zeitschr. fuer Immunitäts Forschung und Experimentelle Therapie*, Vol. 6, Heft 4-5, 1910.)
4. Fruehwald and Weiler: The Modification of Wassermann's Method by Dungers. (*Berl. klin. Wochschr.*, No. 44, 1910.)
5. Muenz: The Wassermann Reaction Made During Office Hours. (*Deutsche med. Wochschr.*, No. 37, 1910.)
6. Pappenheim: As to the Question of the Origin of the Wassermann Reaction. (*Muench. med. Wochschr.*, No. 44, 1910. See in connection, E. Jacobstahl's article in the same number.)
7. Plaut: The Present Status of the Serological Demonstration of Syphilis of the Nervous System. (*Muench. med. Wochschr.*, No. 30, 1907.)
8. Wassermann and Meier: The Clinical Use of the Serum Diagnosis in Lues. (*Deutsche med. Wochschr.*, No. 32, 1907.)

The serum reaction, usually called the Wassermann reaction, will be discussed first in regard to the method itself, and then in regard to the many problems involved as to its worth and value in relation to syphilis. Wassermann utilized the previous method of Bordet in an attempt to apply it, not only in the case of living bacteria, but also to their substances and products. He found by this method that a specific reaction could be evolved which pertained only to the specific substance. After establishing this specificity for a great number of different pathogenic, bacterial and other well-known substances, the nature of which was known, he attempted, on account of its hitherto impossibility, to cultivate or isolate the spirochæta pallida,—the cultivation has lately been made in animals and even in artificial media,—so as to produce a specific reaction, by contact of the substances extracted from the syphilitic tissue with the products of the body present in the serum of syphilitic individuals (antigen and receptors). This was found possible. Though we do not know what the reacting substances are, because of our lack of knowledge as to how to deal directly with the spirochæta, it is a certainty, nevertheless, that they are only present in a syphilitic process.

Wassermann's method is very complicated; in the first place, to follow it requires absolute exactness, and materials, which, under ordinary circumstances, are not only difficult to obtain with facility, but must be kept

under constant control. Hence, this reaction will always be limited to laboratories and to those experimenters who have made a special study of it. According to Noguchi, Dungern and others, all attempts to simplify this method, so that it can be used to its full worth by the general practitioner, have entirely failed; therefore, the only conclusion to be drawn is that the original Wassermann method should be the only one used.

To show the complications which are associated with this method, I shall describe in detail its technique.

The patient's blood is obtained by puncture of one of the veins of the arm, and the quantity should at least be 10 c.c. The serum is poured into tubes which are sealed by means of heat, during the space of twenty minutes at the temperature of 56° C., so that the complement (inactivation) may be destroyed. The antigen is best made from an extract of the liver of a syphilitic fetus. The preferred medium is water, although today alcoholic extracts, which are not as reliable as the aqueous ones, are extensively used. To two parts of the patient's serum are added one part of fresh guinea-pig serum (easily obtained under ether by puncturing the heart) and one part of the extract. Each of these substances is diluted with a salt solution to one c.c. (for 0.2 c.c. of serum). The mixture is then placed in an incubator whose temperature is 37° C., and it is kept there for one hour, so that the complement may eventually be combined with the other substances. Afterwards there is added to the fluid one c.c. of rabbit serum that has been immunized by injecting the red corpuscles of a billy-goat or a nanny-goat (at Johns Hopkins Hospital a sheep is used). Prior to making the Wassermann test, the potency of the fluids should be exactly determined. The last addition is one c.c. of a five per cent. emulsion of red corpuscles from a goat or a sheep. After this is made, the fluid is again placed in an incubator for an hour and a half; then on ice during the night, after which the absence or presence of hemolysis is estimated. If all the materials have been used in the way which I have described, the successful outcome of the test is dependent on the absolute exactness in testing the potency of the antigen and complement, and the patient's serum for hemolysin. Besides this, a control must be made with normal serum by the same procedure. I also usually control with a known syphilitic serum.

The above description cannot but illustrate the difficulty of having all materials on hand at the same time. And here it would be well to emphasize that all alterations of this method, which might tend to facilitate it, are unreliable, especially when alcoholic extracts are used, though these have the quality of remaining unchanged for a long time; hence, to make the test reliable, the extract that is used should be an aqueous one. An aqueous extract can be obtained by thoroughly drying, over sulphuric acid and calcium chloride, finely minced syphilitic tissue, which, when kept cool and deprived of light by being placed in a sealed container, will remain active for several months. The Noguchi improvement on the Wassermann test, which meant the distribution of several substances dried on filter paper, requires, nevertheless, others which cannot be dried (complement and red corpuscles).

To review all that has been written on the subject of the Wassermann test during the last two years is almost impossible. Although my desire has been to get hold of everything published on this subject, I am sure I have overlooked more than two-thirds of the articles. A majority of the reports are quite worthless, since they do not evidence that the results were based on correct examinations. Again, all the reports of cases

examined by methods indicating modifications of the original Wassermann test are far from satisfactory reading. On account of this, I may add, I have noted a tendency in the writings of the last two years to advocate the return to the original Wassermann method. In 1906 Wassermann, Neisser, and Bruck published the first accounts of their observations, but since then the amount of the output on this subject has been so excessive that no human being can follow it. A few articles, however, are of undeniable worth, and from these I intend to quote. Bruck and Stern in their paper recant their former explanation of the reaction by an amboceptor and antigen. They agree with the suggestion of others that the reaction is the effect of a precipitation. Since their object was to contradict what they had previously said, there cannot be any doubt that their interpretation is the correct one. Nevertheless, they insist that a specific substance is present in the reaction, which is only influenced by contact with other substances that allow the first substance to produce the reaction. These substances are of lipoid character, and by combination with cytoplasmic groups cause these to give a positive reaction. Liefman maintains that a precipitation must occur in this reaction, and Jacobsthal asserts that he observed this phenomenon by using the ultramicroscope. Wassermann also reports that the precipitate can be macroscopically demonstrated in the test-tube.

This change of opinion shows that the logical connection of the different findings has not resulted in a thoroughly satisfactory understanding of the agglutination. Besides precipitation, some investigators have found agglutination of the red corpuscles. Hence, the expectation must be that a return to the first explanation of Wassermann's amboceptor and receptor action will be the final result. The whole discussion of the lipoid character of the reaction has not been rewarded by the same consensus of opinion as has the subject of antigens procured from normal organs. Ehrlich's side-chain theory explains this, on account of the receptors not being new formations in the organism due to external influences, but physical and chemical portions of the cells, which serve as a means for the introduction of assimilable bodies with physical and chemical affinities. A definite opinion can be achieved only by studying closely the cultivation of the spirochæta pallida. The outlook from this sort of study has already a hopeful note. Up to the present the cultivated spirochætæ have proved to be avirulent for rabbits and monkeys.

As regards the diagnostic importance of this reaction, the different views as to its value depend upon isolated cases. Syphilis has been diagnosed for so long a time clinically that even to-day, on account of our pursuing similar methods, the reaction is like any other bacterial reaction, in that it is only a confirmatory factor in the diagnosis; of no necessity, for instance, after the spirochæta has been found, or when the signs of the disease are so well marked that a clinical diagnosis is easily effected. Its great value, however, is illustrated in those conditions in which obscure changes, not recognizable by the ordinary methods of diagnosis, suggest a specific causation, or in those cases in which a positive diagnosis cannot be made, on account of the seat of disturbance being so far removed from ocular demonstration that a positive opinion cannot be expressed. To the latter belong all cases of cerebral or spinal syphilis, of syphilis of the bones and the internal organs, and even the lungs. In these doubtful cases the Wassermann reaction is our best means to arrive at a diagnosis; but this fact must not be neglected—namely, the reaction is a systemic one and cannot prove that the suspected lesion is of specific

origin; just as the tuberculin reaction is systemic and not always reactive even in the involved foci in the lung. The Wassermann reaction is declarative only of the presence of active syphilis.

At present, the published reports, as to whether treatment should be influenced by the presence or absence of a positive Wassermann reaction, are unsatisfactory in that a clear interpretation of what should be done cannot be accomplished. This is due to the fact that a large number of these reports contain contradictory statements.

A negative Wassermann reaction may mean a temporary disappearance of the spirochætæ from the lymphatic and vascular structures, but it does not mean that the spirochætæ are not present in lesions of a fibrous character, which are poorly supplied with blood; hence, the conclusion must be that the negativeness of the Wassermann reaction does not indicate that all the spirochætæ are destroyed. In case treatment has been instituted during the first stage of the disease, the reaction may be negative from six to eight weeks afterwards, though two or three months later active secondary lesions or ulcerations may appear. In a case which I saw, the primary lesion dated back fifteen years. Treatment had been administered by injections, inunctions, and internal doses of mercury together with iodide. Treatment covered a period of two and a half years. Until 1909 patient was free from any recurrences and enjoyed good health. He consulted me on June 1st, 1909. The Wassermann reaction was negative. Patient returned on December 6th, 1909, showing massive moist condylomata around the anus with millions of spirochætæ. Similar reports have been made by other observers; therefore, the absence of a positive Wassermann reaction cannot be considered for medical practitioners as an indication that treatment should be stopped. In other words, the Wassermann reaction, whether positive or negative, should not influence the attending physician as to the course of treatment which he ought to pursue. Whether more extensive observations will change this view, it is impossible to say at present. The time, since the reaction was first used, is too short to arrive at any other opinion.

SYPHILIS OF BONE: X-RAY DIAGNOSIS.

REVIEW OF CERTAIN LITERATURE—RECENT AND REMOTE.

By E. H. SKINNER, M. D., of Kansas City.

1. Friedrich: Ueber Knochensyphilis im Roentgenbild. (*Zeitschr. fuer Roentgenkunde,* Band 12, Heft 1. January, 1910.)
2. Horwitz: Differential Points in the Character of the Bone Lesion in the Tuberculous and Acute Osteomyelitis, Rachitis and Syphilis. (*Interstate Med. Jour.,* Vol. XVII., No. 7, July, 1910.)
3. Diefenbach: Roentgen Ray Diagnosis of Diseases of Bone. (*American Quarterly of Roentgenology,* Vol. II., No. 3, September, 1910.)
4. zur Verth: Knochenveraenderungen bei Lues Hereditaria heranwachensender Kinder im Roentgenbild. (*Zentralblatt fuer Roentgenstrahlen,* &c. (Band I., Nr. 9 und 10, pp. 271, November, 1910.)
5. Fritsch: Die "Tibia en lame de sabre" als Folge der erworbenen Lues des Erwachsenen. (*Fort a. d. Gebiete d. Roentgenstrahlen,* Band XVI., Heft I., October, 1910.)
6. Rotch: The Roentgen Ray in Pediatrics. Textbook and Atlas. (J. B. Lippincott Co., 1910.)
7. Spillman: Syphilis Osseuse. (G. Steinheil, Paris, 1909.)
8. Goldthwaite, Painter and Osgood: Diseases of the Bones and Joints. (D. C. Heath & Co., Boston, 1909.)
9. Rumpel: Ueber Geschwuelste und Entzuendliche Erkrankungen der Knochen im Roentgenbild. Atlas. (Lucas, Grafe & Sillem, Hamburg, 1908.)
10. Hahn and Deyche-Pascha: Knochensyphilis im Roentgenbild. (Lucas, Grafe & Sillem, Hamburg, 1907.)
11. Brown: Roentgenological Study of Certain Manifestations of Syphilis. (*Amer. Quar. Roentgenology,* Vol. I., No. 4, July, 1907.)
12. Skinner: Roentgenological Discussion of Bone Lesions. (*Interstate Medical Journal,* Vol. XV., No. 5, May, 1908.)
13. Stadler: Ueber Knochenerkankungen bei Lues Hereditaria tarda. (*Fort. a. d. Gebiete d. Roentgenstrahlen,* Band II., Heft 2, 1907.)
14. Ware: Radiograms of Syphilis of the Long Bones. (*Jour. of Cutaneous Diseases,* Vol. XXV., No. II., November, 1907.)
15. Adami and Nicholls: Principles of Pathology. Vol. II., p. 1029. (Lea & Febiger, 1910.)
16. Preiser: Ueber Knochenveraenderungen bei Lues Congenita tarda. (*Fortschritte a. d. Gebiete d. Roentgenstrahlen,* Band XII., p. 81. 1908.)
17. Haenisch: Beitrag zur Roentgendiagnostik der Knochensyphilis. (*Fortschritte a. d. Gebiete der Roentgenstrahlen.* Band XI., No. 6, 1907.)

18. Koehler: Typische Roentgengramma von Knochengummen. (*Fort. a. d. Gebiete d. Roentgenstrahlen,* Bd. X., No. II., 1907.)

It is possible to project the gross pathological changes of bone-tissues upon the technically perfect *x*-ray negative with astonishing diagnostic satisfaction. By the technically perfect plate we do not necessarily refer to negatives which have been developed to a degree of accuracy and detail obtainable only by experts familiar with photographic chemistry, but to that class of negatives which does provide sufficient bone detail to warrant interpretative probabilities of periosteum, cortex and medulla. Such negatives at the present time are within the reach of almost anyone possessing only ordinary *x*-ray equipment. Good pictures of bone are within the elementary field of *x*-ray effort at the present day. The interpretation of such negatives requires close application and study. A knowledge of the probabilities and possibilities of bone pathology must be the first requisite upon which to base interpretative estimation of the projected pathology displayed upon the *x*-ray negative.

In the interpretation of all negatives, and more especially bone radiographs, it must be remembered axiomatically, that the increased densities due to infiltration, exudation and deposition of osteal cells with inherent lime salts, produce lighter areas upon the negative due to impenetrability by the *x*-ray. Conversely, areas which have lost lime salts, trabeculæ, and their normal densities through erosion, necrosis and osteoporotic processes, show up darker shadows upon the negative, as the *x*-ray readily penetrates these areas. The photographic reproductions or positives of these negatives, of course, show the reverse of these shadows, *i. e.,* all dark spots upon the negative show light upon the prints, and vice versa.

Goldthwaite (8) says: "In the diagnosis of luetic bone- and joint-disease the history of hereditary taint and of venereal lesion or secondary manifestations of the disease are obviously most significantly important. Many of the types will be readily recognized after clinical experience, but here again we have in the *x*-ray our most trustworthy aid in diagnosis, if the technique is good and we train ourselves in the interpretation of these radiographs."

A careful perusal of roentgen literature upon bone syphilis has aroused a suspicion that the various articles have been written around a limited number of observations. This is not surprising, considering the short space of fifteen years which has been given to roentgen diagnosis. The satisfactory element in these various papers and atlasses is the unanimity of diagnostic conclusions, which can be drawn from *x*-ray examinations of syphilitic bone. The classification of syphilitic bone types by the *x*-ray negative can be diagrammatically accomplished by close attention to modern pathological knowledge of the subject under discussion.

The pathological classification of Adami (15) lends itself aptly to the purposes of this discussion. There are the two distinct divisions of *congenital* and *acquired* syphilis. The congenital involvement produces changes in the epiphyseal areas of ossification, and displays itself as an osteochondritis. A proliferative periostitis of the shafts of the long bones is a second division of congenital involvement. The acquired type prefers to attack the periosteum of the long bones with osteoplastic formations or establishes gummatous areas in the periosteum, marrow or cortex of a bone or bones. While included within the category of bone gumma, it is well to call attention to a distinct type of syphilitic osteomyelitis which produces an osteoporosis of the phalanges and the calvarium.

A detailed discussion of the pathology will enable us to interpret our *x*-ray negatives with more satisfaction.

Congenital Syphilis of Bones preferably attacks the epiphyseal lines of ossification in the lower end of the femora. The zone of calcification may become broader and more irregular; the trabecular become thinner with the insertion of islands of cartilage. As the process continues we find the process of ossification more interfered with, the cartilage softens and swells, the epiphyses enlarge and may become separated from the shaft by necrotic areas. In advanced cases, the epiphyses are completely separated and the continued interference with ossification produces a dwarfing of the parts.

A second division of congenital syphilis, entitled *lues hereditaria tarda,* involves the periosteum and corresponds to the tertiary periostitis without gummatous formation of the acquired syphilis. This retarded type involves the periosteum of the long bone shafts. There is marked proliferation of periosteum, with slight involvement of the cortex. No gumma develops, but the constant plastic exudation and proliferation of the osteal layer of the periosteum produces a deformity, simulating a bowing of the bone, which is in reality only a plastic addition to a portion of the bone circumference.

Acquired Syphilis.—Gumma may arise in the periosteum or the bone-marrow. More commonly we meet the localized, flattened, gelatinous elastic swelling. This process may become firm from a granulation process, or produce areas of necrosis similar to caseation. The healing leaves a dense fibrous scar. Periosteal gumma produces considerable erosion and caries of underlying bone, which evolves into an osteoporosis or osteomyelitis syphilitica, and occurs in the phalanges and calvarium with frequency. Gelatinous foci may proceed to purulent necrosis or hyperostosis. Healing may occur by a disappearance of the granulation-tissue and caseous detritis through absorption. The bone may become dense and sclerotic to the density of ivory. Small areas of involvement would probably take the preceding pathological route. If a large area or mass of bone became sequestrated with inflammation of the overlying soft parts, the sequence would probably be: exudation, necrosis, discharge and sinus formation.

Having briefly catalogued the pathology of bone-syphilis, we may turn to the projection of such changes upon the *x*-ray negative. First, we must realize that the *x*-ray casts shadows in direct proportion to the densities of the tissues interposed between the excited *x*-ray tube and the sensitized plate. Second, it is necessary to bring the pathology which we are examining in direct apposition to the plate, to avoid distortion and obtain detail of structure. Positions awkward to the patient are frequently necessary. Third, absolute quietude of the part and repose of the patient must be obtained by sandbags, pillows, compression diaphragms, and supports. Close attention to this latter consideration will produce good diagnostic negatives with slow exposures of small *x*-ray equipments. It should be realized that the mere outline of bone contour, which suffices in some fracture cases, will not give us the information such as a negative showing the detail of periosteal area, cortex, and medulla of bone.

Let us adapt the radiographic discussion to the outline of the pathology of a previous paragraph. The *radiographs of congenital bone-syphilis* show the osseous lesions in direct proportion to the amount of rarefaction or loss of bone-salts in the epiphyseal zone, due to inflammation and necrosis, and the deposit of additional lime salts in the periosteal areas

from a proliferative, osteoplastic process. Usually in children, and more frequently than formerly in adults, the *x*-ray shadows of parts may identify other than mere bone detail and include a record of densities of the periosteum, muscle, fascia and skin. We, therefore, need not conclude that the abnormally increased density of periosteum indicates a shadow of organized bone salts. There is no doubt but that this increased periosteal shadow is due to exudates which eventually form hard bone or syphilitic ivory. Congenital syphilis, while it may involve any joint, is seen most frequently, clinically, in the distal femoral, the distal radial, and the proximal ulnar diaphyses, extending into the zone of ossification. The early case may show merely a rarefaction and loss of lime salts, which may attend the disuse of any bone with an immediate or adjacent inflammation. As the process proceeds, we note further light areas of rarefaction, the trabeculæ of the cancella stand out as distinct lines in the negative, due to the displacement of osteal cells by inflammatory infiltrates. When necrosis eventuates, we note the outlines of the focal breakdown of these trabeculæ and we have the irregular, scalloped, outlined shadow of the necrotic areas. These usually occur in the ends of the diaphysis, first, but extend to the shaft and epiphysis. As syphilitic epiphysitis is usually attended by other osteal involvement; we may find a periostitis of one or more of the long bones, which will serve to differentiate a confused joint picture of syphilis from that of tuberculosis, although usually the tuberculosis is in the epiphysis primarily. This syphilitic necrosis at the diaphysio-epiphyseal junction may lead to complete separation of the epiphysis. The swelling and thickening of the periosteum may lead to the faulty clinical estimation of fracture or dislocation of the epiphysis with callus formation. The *x*-ray negative will provide a correct diagnosis in such cases. Rotch (6, p. 199) mentions having seen cases of separation of the epiphyses in the wrists of infants, which had been mistaken for and treated as fractures, the thickened periosteum being mistaken for a callus. If such separation occurred in syphilis, the erosion of the growth-zone would provide lighter shadows of the areas of necrosis, with darker shadows of the periosteal exudates. In traumatic separation there would be no disturbance of the bone trabeculæ accompanying the displacement, although there might be much similarity between the shadows of periosteal effusion and callus, both being identical processes of nature marshalling her phagocytic army, the former for offense and the latter for defense.

Besides the periosteal effort in the neighborhood of congenital joint-syphilis, we may encounter a periostitis of the long bones, which may be a complication of the joint or a separate syphilitic demonstration. As a distinct entity it is usually presented to our attention in the sabre tibia. The condition of sabre tibia is a frequent development of the tertiary period of acquired syphilis, and is considered as an evidence of retarded syphilitic manifestation in the congenital. The course is one of periosteal effusion, exudation, infiltration, hyperostosis and deposition of osteal cells, which, in turn, is followed by an ivory sclerosis. There is a certain amount of gummatous infiltration of the cortex from the contiguous periosteal involvement. The bowing of the tibia is described by Fritsch (5) as due to more sclerotic change than is necessary to replace the gummatous periostitis, which promotes a crimping or buckling of the tibia, as the fibula is usually not concerned, the fibula maintains the length of the leg. The radiograph shows a normal fibula, but the tibia presents darker shadows of the portion of the tibia involved. It appears as if bone substance has been plastered upon portions of its circumference. Ware

(14) states that where this tibial circumferential thickening is upon a portion of the bone contiguous to the interosseous space, it could only be accurately recognized by the radiograph, and contends, in contradistinction to Fritsch, that the sclerosis following a gummatous peristostitis plus a growth of the length of the bone, due to irritation, with the fibula maintaining the normal length, produces the bowing of the tibia. A similar phenomenon in the bones of the forearm is often encountered.

The *radiographic diagnosis of acquired syphilis* will depend upon the amount of osteal involvement. We usually look for these tertiary complications in the tubular bones of the legs and arms and the plates of the skull. The syphilitic invasion of the nose and palate, because of their anatomical locations, do not lend themselves to *x*-ray demonstration. The latter are usually so evident by inspection and palpation that the *x*-ray offers nothing of value.

The syphilitic attack upon periosteum primarily displays itself radiographically by a cloudy shadow of the periosteal area, which is broader than normal. As the process increases we note a more distinct outline of the periosteum, with flecks of ossifying centres. If the process does not recede, we find that this ossification of the exudate resembles a layer of plaster upon the normal contour of the bone. If the cortex has become involved, without the formation of distinct areas of gummatous degeneration, this plaster process casts dense shadows, showing the osteosclerosis of cortical and periosteal areas. Where the cortex beneath an involved periosteum develops gummata, these gummata will appear as lighter spots surrounded by a darker zone of inflammatory exudate. The changes described in this paragraph are usually displayed in the tubular bones of the leg and forearm. Friedrich (1) states that a characteristic roentgen finding in syphilis is the combination of a gummatous periostitis and ostitis, with an ossifying periostitis and ostitis; an osteoporosis plus an osteoplastic process.

Osteomyelitis Syphilitica, while it may develop as an extension of gummatous periostitis, will most frequently be found as a primary medullary invasion. The most startling demonstration is found in the plates of the skull. The flat bones of the cranium may take on a diffuse sclerosis with osteoplastic processes, but generally an osteoporotic change, with extending suppuration and eventually perforation occurs. Small islands of bone may form which later may be discharged as sequestra with the formation of perforations in the skull plates. The *x*-ray findings in an osteoporosis of the skull are conclusive; the thickening and plastic growth of the periosteum will be displayed by an increased shadow of this area; the porotic changes will be outlined by increased radiability; the islands of degenerated bone give the plate an appearance of irregular lace-work.

The syphilitic osteomyelitis of the long bones, particularly the femur and humerus, may give rise to few subjective symptoms aside from pain and impaired function, and the condition will not be discovered until a spontaneous fracture occurs, unless the *x*-ray is used. The *x*-ray reveals the osteoporosis of the medulla and cortex, with not the amount of periosteal infiltration and thickening that accompanies a primary periostitis gummatosa. The bone upon the *x*-ray plate appears honey-combed and flecked with dark and light areas of porotic changes. The differential diagnosis between sarcoma, myeloma, and septic osteomyelitis is eminent. The latter may be excluded by the pain characteristics, temperature record, and blood count. Syphilitic osteomyelitis is confined to the normal shaft area of the bone which, with periosteal thickening, produces a

fusiform shadow. Sarcoma will usually break through the periosteum and invade the soft parts. Further, appropriate internal medication will promote the healing of the syphilitic case in a space of time insufficient to allow of much progress in a sarcoma.

Syphilitic dactylitis is encountered in the metacarpal and phalangeal bones. It is readily differentiated from the tubercular dactylitis by the fact that syphilis appears to veil the bone with several layers of periosteal plastic overgrowth, while the tuberculosis involves the medullary portion, forming a necrotic area which is easily recognized by the *x*-ray.

Charcot Joint.—Inasmuch as we now attribute almost all cases of tabes dorsalis to syphilis, this may be regarded as a tertiary manifestation of acquired syphilis. The *x*-ray negative displays the rarefaction and atrophic erosion of the articular extremities of a joint, with the deposit of calcareous debris within the distended joint confines. Luxations of the joint frequently prevails. Brown (11) states that "the exuberant bone formation may involve the capsule, synovia, ligaments, tendons and muscle attachments, which shadows may obliterate the atrophy obtaining in the articular extremities." It must be realized that while the majority of Charcot joints are presented in the knee, this condition may occur in other joints, particularly of the ankle and elbow.

General Considerations. zur Verth (4) draws attention to a transverse line shadow in the diaphysis running parallel to the epiphyseal line, which displayed itself in the tibial head of a case which subsequently developed a syphilitic spina ventosa of metacarpal phalangeal bone. Also, while not disparaging the contention of Rumpel (9), Hahn and Deyche-Pascha (10) that general bone atrophy is a manifestation of congenital syphilis, he believes with Preiser (16) that this bone atrophy is distal to luetic lesions, but when universally distributed in the bones of the body is indicative of rachitis. zur Verth considers that evidence of keratitis parenchymata and a positive Wassermann reaction are elements that demand attention in the interpretation of radiographs.

Haenisch (17) reports two cases in which the "diagnosis of bone syphilis was accomplished and calls attention to the desirability of making *x*-ray exposures of the lesion at intervals to determine whether anti-syphilitic treatment of a given case is promoting a recession of the bone involvement." Where the differentiation between sarcoma and syphilitic osteoporosis was doubtful, it would be possible to note within a month's course of the iodides, mercury, or now "606," whether there was change for the better.

Horwitz (2) gives some good axiomatic points of differentiating the bone lesions of syphilis, rickets, tuberculosis, and osteomyelitis. We quote (with some liberties): "Osteomyelitis and syphilis may be termed constructive; rickets and tuberculosis, destructive. Tuberculosis attacks the epiphysis and only, secondarily, enters the diaphysis; osteomyelitis, shaft first and epiphysis by extension. Syphilis has predilection for periosteum, showing irritation and consequent proliferation. Rickets shows thickening of cortex, always upon the concavity of the bone; syphilis usually shows thickening upon all sides. Osteomyelitis and acquired syphilis show comparative freedom of joint involvement. Congenital syphilis, on the contrary, presents unilateral osteochondritis of the growth zone."

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PARIS LETTER.

THE RÔLE OF SYPHILIS IN VISCERAL PATHOLOGY.

By Auguste A. Housquains, M. D.

Only a few years ago, syphilis was defined either as an indurated chancre, a secondary eruption, or as a gumma. The inoculation of animals, the discovery of the pathogenic agent, the study of serum reactions, the progress in the therapy and clinical analysis, all these advances, have greatly widened our knowledge of syphilis. To-day we are aware of the fact that a thorough study of syphilis should be made in chronic visceral lesions, in lesions of the central nervous system, such as tabes, general paralysis, and hemorrhage; in lesions of the liver and kidneys, and in diseases of the stomach.

Formerly these affections were considered completely independent of syphilis; but directly we became convinced of their frequent coincidence with syphilis the expression, parasyphilitic, was created to indicate the non-specific character of their pathological histology. This expression, however, is not considered accurate at the present time. In fact, it is no longer thought doubtful that these chronic visceral lesions are due to syphlis, since their pathological histology can be traced back to the presence at one time of the initial lesion. The study of chronic infections has demonstrated to us that all microbian diseases can assume aspects which have nothing characteristic from the standpoint of etiology. Thus tuberculosis, for example, which at times assumes the form of septicemia so decidedly that at an autopsy no trace of a tubercle can be found, may cause the ordinary attacks of cirrhosis of the liver and nephritis. Nevertheless, these lesions are of tuberculous origin, according to our clinical and bacteriological teachings. It is absolutely the same in syphilis; hence, it is not reasonable to call the lesions, which are undoubtedly directly dependent on the primary sore, parasyphilitic.

The study of the histopathological processes in syphilis is of the greatest interest, but the matter of specificity plays no part in these processes, if a truthful statement be made. Nevertheless, there exists a combination of sufficiently different characteristics which permits us to recognize a syphilitic lesion.

In the first place, there is a period of incubation during which the treponemæ vegetate locally. This is the intra-epithelial period. Then the infectious agent passes through the epidermis, attacks the vessels, becomes general throughout the system, and is again seen in the first exanthem.

Afterwards, the syphilitic agent manifests itself, in a histological sense, by causing divers lesions: a dermic filtrate in the manner of papules; a syphilitic folliculitis, which is nothing else than a gumma; and an arteritis and a phlebitis. On a level with the surface of the viscera, a cell can be affected by syphilis without there being an arteritis; however, arteritis is present in the majority of visceral syphilitic changes. The cure is best effected by a fatty, granular degeneration, or better by a fibro-sclerotic transformation. These changes take place in the brain, marrow, kidneys and liver, and cause the continued destruction of the healthy elements of the tissues.

These indications illustrate that there is no interruption in the evolution of histological alterations, and consequently, that there is a continuity in the development and the connection of the various clinical manifestations of syphilis. Let us take, for example, the nervous disturbances classed under the name of parasyphilitic affections. The recent work of Babinski, Widal, Nageotte, and Ravaut has demonstrated that these nervous disturbances are frequently preceded by a chronic meningitis of a syphilitic nature. Therefore it would be wrong to say that in these cases there was an interruption between the secondary period and the morbid phenomena which appeared later on. Without doubt, chronic syphilitic meningitis can remain latent, and it is possible to disclose the true nature of the disease if a thorough study is brought to bear upon it.

It is true that this sort of research is not always easy to make, for it is rather difficult to prove in the living that chronic meningitis is the certain intermediary between recognized nervous troubles and a previous syphilis. "In order to prove this," says Clovis Vincent, "it is necessary to make, from time to time, a lumbar puncture in all those syphilitics who appear to be free from nerve lesions." But, as we all know, when a patient has no pains he refuses almost always to submit to any procedure. Therefore, a lumbar puncture is hardly ever made until the appearance of acute nervous disturbances. But the verification of the diagnosis of meningitis made by means of a lumbar puncture does not imply that the meningitis preceded the nervous disturbances. Nevertheless, even in these cases Clovis Vincent believes that we ought to admit that chronic meningitis had already existed. He bases his opinion on the fact that, whenever he has had occasion to examine patients presenting nervous disturbances which could be imputed to syphilis, at a time when the nervous disturbances were in their incipiency, the lumbar puncture revealed a rachidian lymphocytosis. Following this opinion, he has punctured syphilitics afflicted with hemaplegia, directly there was icterus, others having simply a lingual hemiatrophy, paralysis of the third, sixth, and eighth pairs of nerves, and even those patients who presented only one symptom—the Argyll-Robertson pupil. In all these cases he found considerable meningeal reaction. Other observers have already made similar assertions; hence, from the ensemble of these facts we gather that all nervous disturbances of syphilitic origin are accompanied by meningitis. The three cases of Vincent indicate the fact of the anteriority of meningitis. These cases were three well-marked examples of syphilis in which the diagnosis of meningitis could be well established before the appearance of the nervous disturbances, and this was done by means of the lumbar puncture. In one of the cases was observed, somewhat later, a progressive general paralysis; in the second, a tetraplegia with a pseudobulbar syndrome; in the third, a neuritis of the eighth cranial pair of nerves with bilateral deafness.

Thus we can understand how an old syphilis can develop a general paralysis or tabes, some years after the appearance of the initial lesion. This is due to a meningitis in a state of slow but uninterrupted evolution, by which gradual changes are produced in the nerve elements. Hence the physician should regard those patients who, after the disappearance of the secondary eruption, continue to present a cephalorachidian lymphocytosis, as special subjects for nervous disturbances. The therapeutic conclusion is this: we should continue to administer the antisyphilitic treatment in these cases as long as the lumbar puncture yields a positive result.

It is highly probable that the condition, which is caused by lesions of the central nervous system, can be reproduced when there are chronic changes in the viscera: diseases of the liver, kidneys, and lungs that supervene later on in patients who have had syphilis for a number of years. There is undoubtedly an intermediary stage which cannot be recognized at the time by the physician, but during which alterations in these organs take place. As regards the nerve lesions, we are justified in saying that the arterial constitute the most formidable complications of syphilis. The study of chronic aortitis, in particular, if one analyzes it in connection with syphilitic infection, offers a subject of the greatest interest. Syphilis can, in fact, cause in the secondary and tertiary stages changes which are easily recognized as specific, or later on lesions that have the ordinary aspect of arteritis, atheroma, and aneurysm: diseases which at first sight would not be attributed by the physician to syphilis, but which, by means of more extensive study and the employ of laboratory methods, prove to be of syphilitic origin. These lesions are in reality much older than they appear to be. They are present prior to the time when the first clinical manifestations become apparent; in fact, they date from the time the treponemæ penetrate into the blood, just as tabes, which is a later complication of syphilis, has its anatomical beginning in the latent meningitis of the secondary period. If, in any of these cases, there is any doubt as to the symptoms being due to a former syphilis, the laboratory methods will lend considerable support to any clinical deficiency, and the Wassermann reaction can be of the greatest service. Debove does not hesitate to say that chronic aortitis has a diagnostic value in arriving at the conclusion of the existence of an old syphilis. Its coincidence with the nervous disturbances suffices, from his point of view, to show the fact of their syphilitic origin.

Although the facts mentioned above are not, as yet, absolute certainties, the number and value of the observations upon which these facts are based constitute presumptions which should impress all of us as to their worth and value. In all the cases in which my doctrine of parasyphilis has been adopted, it has rendered considerable service as regards the grouping of facts, the interpreting of them and the furthering of more and more careful researches. Furthermore, the explanation of the delayed complications in the last stages of the evolution of syphilis is simple enough to make us hopeful that the lesson will be understood by all physicians. The connecting links in the chain reach uninterruptedly from the last complications to the initial lesion; and though we have hitherto denied this on account of our incapacity to demonstrate each and every step, our present attitude is such that we are in a position to recognize the importance of the rôle of syphilis in the pathogenesis of a large number of chronic visceral diseases.

December 10th.

BOOK REVIEWS.

NERVOUS STATES. By Dr. Paul Dubois, Professor of Neuropathology in the University of Berne; Author of "The Psychic Treatment of Nervous Disorders," "The Influence of the Mind on the Body," etc. New York; Funk & Wagnalls Co. 1910.

This book is very Doboisesque and is the concentration of the ideas of that master of neurologic theology. The vogue of Dubois and his special kind of psychotherapy is perhaps passing, but, nevertheless, anything from his pen is of interest. Dubois, compared with the vigorous and vital conception of Freud, seems tame, but at the same time there is no doubt that there is a place in therapeutics for his method, which is practically that of personal influence and persuasion. If his larger book pales a little and seems needlessly diffuse and preachy, this miniature will be in a refreshing contrast. "Nervous States" can therefore be recommended as an easy sermon on how to cure a patient by the method of talking him out of it. Loquaciousness as a therapeutic agency has yet to be developed; perhaps this book is the beginning.

HANDBOOK OF PHYSIOLOGY. By W. D. Halliburton, M. D., L. L. D., F. R. C. P., F. R. S., Professor of Physiology, King's College, London. Ninth Edition (being the twenty-second edition of Kirkes' Physiology), with nearly six hundred illustrations in the text, many of which are colored, and three colored plates. Philadelphia: P. Blakiston's Son & Co., 1910. Price, $3.00.

The new edition of this work fully demonstrates the painstaking care of the author in his endeavor to bring the subject-matter up to date. Most of the chapters have been entirely rewritten. The greatest change is seen in the sections dealing with the physiology of the central nervous system and the ductless glands. The chapters on the physiology of the brain, especially, have been changed in accordance with the results of modern research. The book is well illustrated; the style logical and clear. The work, as a whole, will undoubtedly prove a source of pleasure as well as advanced instruction to every student of physiology.

PRACTICAL NURSING—FOR MALE NURSES IN THE R. A. M. C. AND OTHER FORCES. By Major E. M. Hassard, R. A. M. C., and A. R. Hassard. New York: Oxford University Press. 1910. Price, $1.50.

In a book for army nurses, such as this, the instruction in what to do in emergencies is necessarily more detailed than in textbooks for hospital nurses. The description of the various first-aid procedures is full and clear and may well meet the requirements of the young practitioner as well as of the male nurse. Under the circumstances, too, it is not surprising that much space is given to tropical diseases.

HYGIENE AND PUBLIC HEALTH. By B. Arthur Whitelegge and George Newman. Illustrated. New York: Funk and Wagnalls Company. 1910.

This manual provides a concise summary of the current knowledge concerning public health for the purposes of the health officer, as well as an elementary textbook for the student. The conditions discussed in it are primarily those obtaining in England, but this makes it if anything even more suggestive to the American. In many respects, it is clear, the English manage their public hygiene better than we.

NEUE FORSCHUNGEN AUF DEM GEBIETE DER INTESTINALEN AUTOINTOXIKATIONEN UND IHRE BEHANDLUNG. Von Sanitaetsrat Dr. C. Wegele. Wuerzburger Abhandlungen aus dem Gesamtgebiet der praktischen Medizin. X. Band. 8 Heft. Wuerzburg: Curt Kabitzsch (A. Stuber's Verlag). 1910. Price, 85 pf.

A critical review by an eminent clinician of recent work in intestinal autointoxication.